

This Page Is Inserted by IFW Operations
and is not a part of the Official Record

BEST AVAILABLE IMAGES

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images may include (but are not limited to):

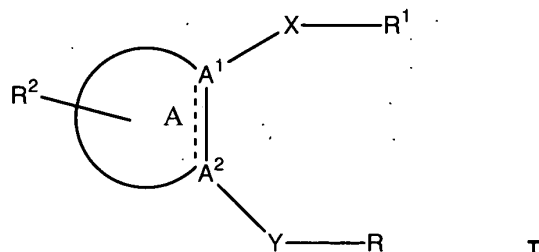
- BLACK BORDERS
- TEXT CUT OFF AT TOP, BOTTOM OR SIDES
- FADED TEXT
- ILLEGIBLE TEXT
- SKEWED/SLANTED IMAGES
- COLORED PHOTOS
- BLACK OR VERY BLACK AND WHITE DARK PHOTOS
- GRAY SCALE DOCUMENTS

IMAGES ARE BEST AVAILABLE COPY.

**As rescanning documents *will not* correct images,
please do not report the images to the
Image Problem Mailbox.**

WHAT IS CLAIMED IS:

1. A compound of formula I

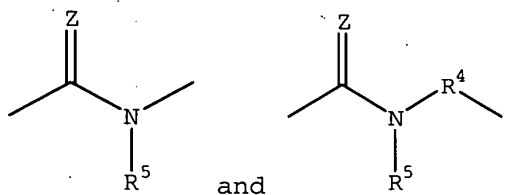


wherein each of A¹ and A² is independently C, or N;

wherein ring A is selected from

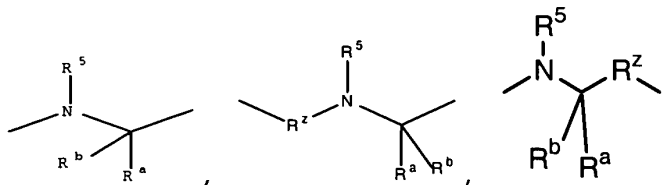
- a) 5- or 6-membered partially saturated heterocyclyl,
- b) 5- or 6-membered heteroaryl,
- c) 9- or 10-membered fused partially saturated heterocyclyl,
- d) 9-, 10- or 11-membered fused heteroaryl;
- e) naphthyl, and
- f) 4-, 5- or 6- membered cycloalkenyl;

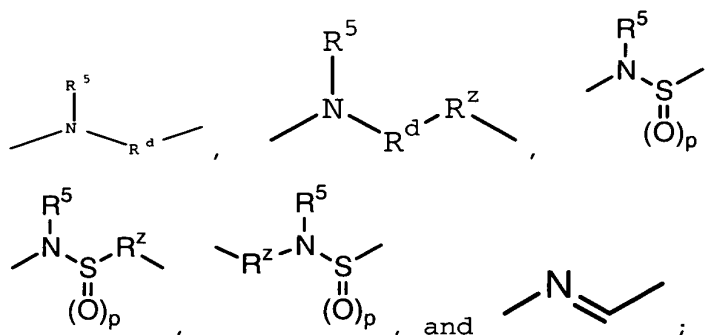
wherein X is selected from



wherein Z is oxygen or sulfur;

wherein Y is selected from





wherein p is 0 to 2,

wherein R^a and R^b are independently selected from H, halo,

5 cyano, $-NHR^6$ and C_{1-4} -alkyl substituted with R^2 , or wherein R^a and R^b together form C_3 - C_6 cycloalkyl;

wherein R^z is selected from C_1 - C_4 alkylene, where one of the CH_2 groups may be substituted with an oxygen atom or an -NH-;

10 wherein R^d is cycloalkyl;

wherein R is selected from

a) substituted or unsubstituted 5-6 membered heterocyclyl, and

b) substituted or unsubstituted fused 9-, 10- or 11- membered heterocyclyl;

15 wherein substituted R is substituted with one or more substituents independently selected from halo, $-OR^3$, $-SR^3$, $-SO_2R^3$, $-CO_2R^3$, $-CONR^3R^3$, $-COR^3$, $-NR^3R^3$, $-SO_2NR^3R^3$, $-NR^3C(O)OR^3$, $-NR^3C(O)R^3$, cycloalkyl, optionally substituted 5-6 membered heterocyclyl, optionally substituted phenyl, lower alkyl substituted with R^2 , cyano, nitro, lower alkenyl and lower alkynyl;

wherein R^1 is selected from

a) substituted or unsubstituted 6-10 membered aryl,

25 b) substituted or unsubstituted 5-6 membered heterocyclyl,

c) substituted or unsubstituted 9-11 membered fused heterocyclyl,

2025 RELEASE UNDER E.O. 14176

d) cycloalkyl, and

e) cycloalkenyl,

wherein substituted R¹ is substituted with one or more substituents independently selected from halo, -OR³,
5 -SR³, -CO₂R³, -CONR³R³, -COR³, -NR³R³, -NH(C₁-C₄ alkylenylR¹⁴), -SO₂R³, -SO₂NR³R³, -NR³C(O)OR³, -NR³C(O)R³, optionally substituted cycloalkyl, optionally substituted 5-6 membered heterocyclyl, optionally substituted phenyl, lower alkyl
10 substituted with R², cyano, nitro, lower alkenyl and lower alkynyl;

wherein R² is one or more substituents independently selected from H, halo, -OR³, oxo, -SR³, -CO₂R³, -COR³, -CONR³R³, -NR³R³, -SO₂NR³R³, -NR³C(O)OR³, -NR³C(O)R³, cycloalkyl,
15 optionally substituted phenylalkylenyl, optionally substituted 5-6 membered heterocyclyl, optionally substituted heteroarylalkylenyl, optionally substituted phenyl, lower alkyl, cyano, lower hydroxyalkyl, lower carboxyalkyl, nitro, lower alkenyl, lower alkynyl, lower aminoalkyl, lower alkylaminoalkyl and lower haloalkyl;
20 wherein R³ is independently selected from H, lower alkyl, phenyl, 5-6 membered heterocyclyl, C₃-C₆ cycloalkyl, and lower haloalkyl;

wherein R⁴ is independently selected from C₂-C₄ alkylenyl, C₂-C₄ alkenylenyl and C₂-C₄ alkynylenyl, where one of the CH₂ groups may be substituted with an oxygen atom or an -NH-;
25

wherein R⁵ is selected from H, lower alkyl, phenyl and lower aralkyl; and

30 wherein R⁶ is selected from H or C₁₋₆-alkyl;

wherein R¹⁴ is selected from H, phenyl, 5-6 membered heterocyclyl and C₃-C₆ cycloalkyl;

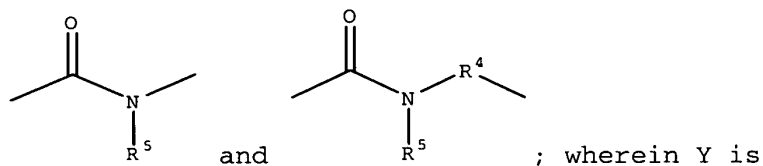
and pharmaceutically acceptable salts thereof;

404565-04-0000

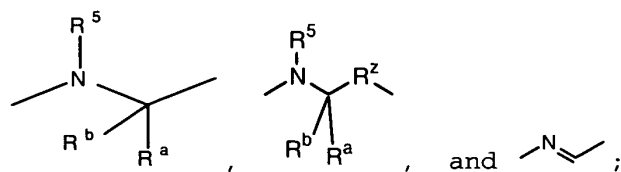
provided A is not naphthyl when X is -C(O)NH- and when R¹ is phenyl when Y is -NHCH₂- and when R is 4-pyridyl; further provided A is not pyridyl when X is -C(O)NH- and when Y is -NHCH₂- and when R is 4-pyridylpiperidin-4-yl, 1-tertbutylpiperidin-4-yl, 1-isopropylpiperidin-4-yl or 1-cycloalkylpiperidin-4-yl; further provided A is not pyridyl when X is -C(O)NH- and when R¹ is 4-[3-(3-pyridyl)-5-(trifluoromethyl)-1H-pyrazol-1-yl]phenyl when Y is -NHCH₂- and when R is 4-pyridyl; and further provided R is not unsubstituted 2-thienyl, 2-pyridyl or 3-pyridyl when Y is -NHCH₂-.

2. Compound of Claim 1, and pharmaceutically acceptable salts thereof, wherein A is selected from 5- or 6- membered partially saturated heterocyclyl.

3. Compound of Claim 2, and pharmaceutically acceptable salts thereof, wherein A is selected from dihydropyran, dihydrothienyl, dihydrofuryl, oxo-dihydrofuryl, pyrrolinyl, dihydrothiazolyl, dihydro-oxazolyl, dihydro-isothiazolyl, dihydro-isoxazolyl, imidazolynyl and pyrazolynyl; wherein X is selected from



selected from



wherein R^a and R^b are independently selected from H, halo, cyano, and C₁₋₂-alkyl substituted with R², or wherein R^a and R^b together form C₃-C₄ cycloalkyl; wherein R² is C₁-C₂

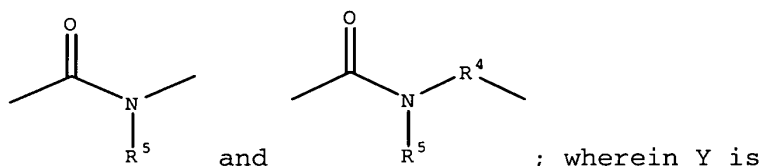
alkylenyl, where one of the CH₂ groups may be substituted with an oxygen atom or an -NH-; wherein R is selected from substituted or unsubstituted 5-6 membered heteroaryl comprising one or more nitrogen atoms, and substituted or unsubstituted 9-10 membered fused heteroaryl comprising one or more nitrogen atoms; wherein substituted R is substituted with one or more substituents independently selected from halo, -OR³, -SR³, -CO₂R³, -CONR³R³, -COR³, -NR³R³, -SO₂NR³R³, -NR³C(O)OR³, -NR³C(O)R³, cycloalkyl, optionally substituted 5-6 membered heterocyclyl, optionally substituted phenyl, C₁₋₂-alkyl, cyano, C₁₋₂-hydroxyalkyl, nitro and C₁₋₂-haloalkyl; wherein R¹ is selected from substituted or unsubstituted aryl selected from phenyl, naphthyl, indenyl and tetrahydronaphthyl, substituted or unsubstituted 5-6 membered heteroaryl, and substituted or unsubstituted 9-10 membered fused heteroaryl; wherein substituted R¹ is substituted with one or more substituents independently selected from halo, -OR³, -SR³, -SO₂R³, -CO₂R³, -CONR³R³, -COR³, -NR³R³, -NH(C₁₋₂ alkylenylR³), -(C₁₋₂ alkylenyl)NR³R³, -SO₂NR³R³, -NR³C(O)OR³, -NR³C(O)R³, optionally substituted cycloalkyl, optionally substituted 5-6 membered heterocyclyl, optionally substituted phenyl, optionally substituted phenyl-C₁₋₂-alkylenyl, optionally substituted 5-6 membered heterocyclyl-C₁₋₂-alkylenyl, C₁₋₂-alkyl, cyano, C₁₋₂-hydroxyalkyl, nitro and C₁₋₂-haloalkyl; wherein R² is one or more substituents independently selected from H, halo, -OR³, oxo, -SR³, -CO₂R³, -CONR³R³, -COR³, -NR³R³, -SO₂NR³R³, -NR³C(O)OR³, -NR³C(O)R³, cycloalkyl, optionally substituted 5-6 membered heterocyclyl, optionally substituted phenyl, C₁₋₂-alkyl, cyano, C₁₋₂-hydroxyalkyl, C₁₋₃-carboxyalkyl, nitro, C₂₋₃-alkenyl, C₂₋₃-alkynyl and C₁₋₂-haloalkyl; wherein R³ is selected from H, C₁₋₂-alkyl, phenyl, C₃-C₆ cycloalkyl and C₁₋₂-haloalkyl; wherein R⁴ is C₂₋₃-alkylenyl, where one of the CH₂

2025 RELEASE UNDER E.O. 14176

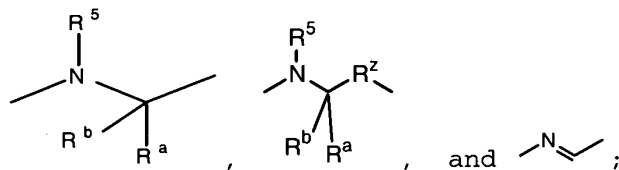
groups may be substituted with an oxygen atom or an -NH-;
and wherein R⁵ is selected from H and C₁₋₂-alkyl.

4. Compound of Claim 1, and pharmaceutically
5 acceptable salts thereof, wherein A is selected from 5- or
6- membered heteroaryl.

5. Compound of Claim 4, and pharmaceutically
acceptable salts thereof, wherein A is selected from
10 pyridyl, pyrazinyl, pyrimidinyl, pyridazinyl, triazinyl,
thienyl, furanyl, pyrrolyl, thiazolyl, oxazolyl, imidazolyl,
pyrazolyl, isoxazolyl, triazolyl and isothiazolyl; wherein X
is selected from



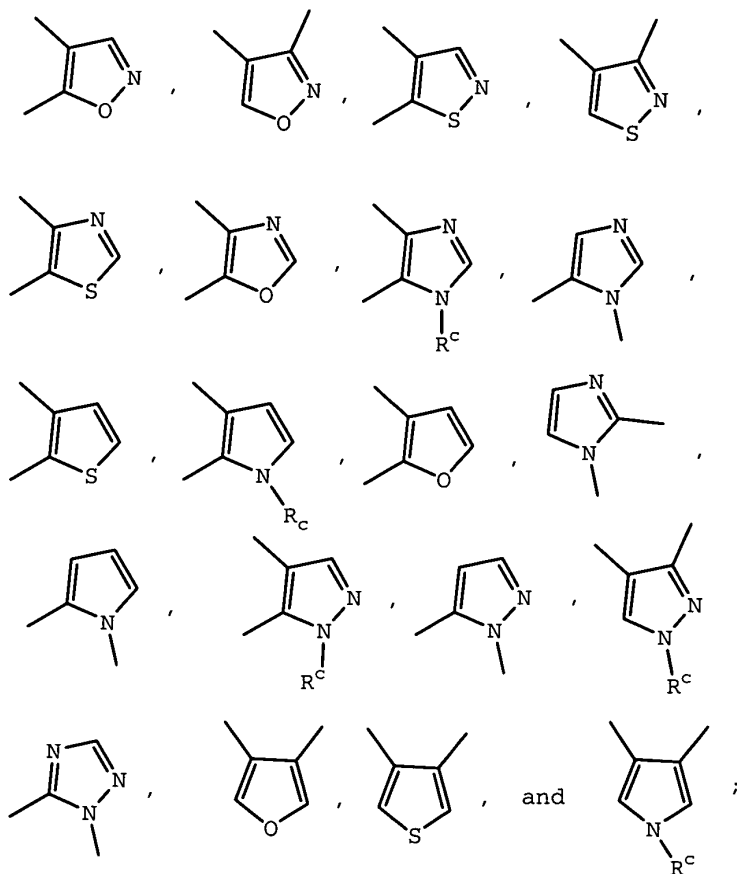
- 15 selected from



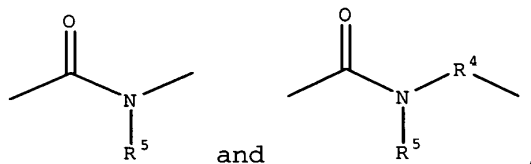
- wherein R^a and R^b are independently selected from H, halo,
cyano, and C₁₋₂-alkyl substituted with R², or wherein R^a and
R^b together form C₃-C₄ cycloalkyl; wherein R^z is C₁-C₂
20 alkylene, where one of the CH₂ groups may be substituted
with an oxygen atom or an -NH-; wherein R is selected from
substituted or unsubstituted 5-6 membered heteroaryl
comprising one or more nitrogen atoms, and substituted or
unsubstituted 9-10 membered fused heteroaryl comprising one
25 or more nitrogen atoms; wherein substituted R is substituted
with one or more substituents independently selected from
halo, -OR³, -SR³, -CO₂R³, -CONR³R³, -COR³, -NR³R³, -SO₂NR³R³, -
NR³C(O)OR³, -NR³C(O)R³, cycloalkyl, optionally substituted 5-

- 6 membered heterocyclyl, optionally substituted phenyl, C₁₋₂-alkyl, cyano, C₁₋₂-hydroxyalkyl, nitro and C₁₋₂-haloalkyl; wherein R¹ is selected from substituted or unsubstituted aryl selected from phenyl, naphthyl, indenyl and
- 5 tetrahydronaphthyl, substituted or unsubstituted 5-6 membered heteroaryl, and substituted or unsubstituted 9-10 membered fused heteroaryl; wherein substituted R¹ is substituted with one or more substituents independently selected from halo, -OR³, -SR³, -SO₂R³, -CO₂R³, -CONR³R³, -
- 10 COR³, -NR³R³, -NH(C₁-C₂ alkyleneR³), -(C₁-C₂ alkylene)NR³R³, -SO₂NR³R³, -NR³C(O)OR³, -NR³C(O)R³, optionally substituted cycloalkyl, optionally substituted 5-6 membered heterocyclyl, optionally substituted phenyl, optionally substituted phenyl-C₁₋₂-alkylene, optionally substituted 5-6
- 15 membered heterocyclyl-C₁-C₂-alkylene, C₁₋₂-alkyl, cyano, C₁₋₂-hydroxyalkyl, nitro and C₁₋₂-haloalkyl; wherein R² is one or more substituents independently selected from H, halo, -OR³, oxo, -SR³, -CO₂R³, -CONR³R³, -COR³, -NR³R³, -SO₂NR³R³, -NR³C(O)OR³, -NR³C(O)R³, cycloalkyl, optionally substituted 5-
- 20 6 membered heterocyclyl, optionally substituted phenyl, C₁₋₂-alkyl, cyano, C₁₋₂-hydroxyalkyl, C₁₋₃-carboxyalkyl, nitro, C₂₋₃-alkenyl, C₂₋₃-alkynyl and C₁₋₂-haloalkyl; wherein R³ is selected from H, C₁₋₂-alkyl, phenyl, C₃-C₆ cycloalkyl and C₁₋₂-haloalkyl; wherein R⁴ is C₂₋₃-alkylene, where one of the CH₂
- 25 groups may be substituted with an oxygen atom or an -NH-; and wherein R⁵ is selected from H and C₁₋₂-alkyl.

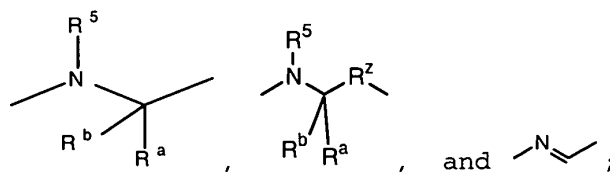
6. Compound of Claim 1 wherein A is selected from



wherein R^c is selected from H, methyl and optionally
 5 substituted phenyl; wherein X is selected from



wherein Y is selected from



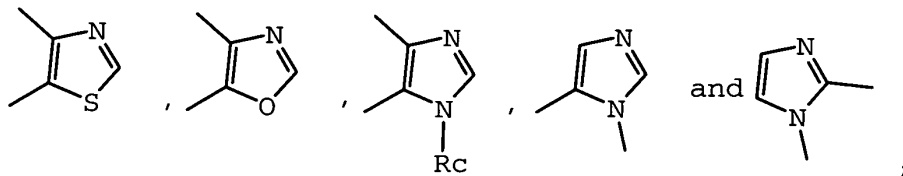
wherein R^a and R^b are independently selected from H, halo,
 10 cyano, and C_{1-2} -alkyl substituted with R^2 , or wherein R^a and
 R^b together form C_3-C_4 cycloalkyl; wherein R^z is C_1-C_2
 alkylenyl, where one of the CH_2 groups may be substituted

4004564 044000

with an oxygen atom or an -NH-; wherein R is selected from substituted or unsubstituted 5-6 membered heteroaryl comprising one or more nitrogen atoms, and substituted or unsubstituted 9-10 membered fused heteroaryl comprising one or more nitrogen atoms; wherein substituted R is substituted with one or more substituents independently selected from halo, -OR³, -SR³, -CO₂R³, -CONR³R³, -COR³, -NR³R³, -SO₂NR³R³, -NR³C(O)OR³, -NR³C(O)R³, cycloalkyl, optionally substituted 5-6 membered heterocyclyl, optionally substituted phenyl, C₁₋₂-alkyl, cyano, C₁₋₂-hydroxyalkyl, nitro and C₁₋₂-haloalkyl; wherein R¹ is selected from substituted or unsubstituted aryl selected from phenyl, naphthyl, indenyl and tetrahydronaphthyl, substituted or unsubstituted 5-6 membered heteroaryl, and substituted or unsubstituted 9-10 membered fused heteroaryl; wherein substituted R¹ is substituted with one or more substituents independently selected from halo, -OR³, -SR³, -SO₂R³, -CO₂R³, -CONR³R³, -COR³, -NR³R³, -NH(C₁-C₂ alkyleneR³), -(C₁-C₂ alkylene)NR³R³, -SO₂NR³R³, -NR³C(O)OR³, -NR³C(O)R³, optionally substituted cycloalkyl, optionally substituted 5-6 membered heterocyclyl, optionally substituted phenyl, optionally substituted phenyl-C₁₋₂-alkylene, optionally substituted 5-6 membered heterocyclyl-C₁₋₂-alkylene, C₁₋₂-alkyl, cyano, C₁₋₂-hydroxyalkyl, nitro and C₁₋₂-haloalkyl; wherein R² is one or more substituents independently selected from H, halo, -OR³, oxo, -SR³, -CO₂R³, -CONR³R³, -COR³, -NR³R³, -SO₂NR³R³, -NR³C(O)OR³, -NR³C(O)R³, cycloalkyl, optionally substituted 5-6 membered heterocyclyl, optionally substituted phenyl, C₁₋₂-alkyl, cyano, C₁₋₂-hydroxyalkyl, C₁₋₃-carboxyalkyl, nitro, C₂₋₃-alkenyl, C₂₋₃-alkynyl and C₁₋₂-haloalkyl; wherein R³ is selected from H, C₁₋₂-alkyl, phenyl, C₃-C₆ cycloalkyl and C₁₋₂-haloalkyl; wherein R⁴ is C₂₋₃-alkylene, where one of the CH₂ groups may be substituted with an oxygen atom or an -NH-; and wherein R⁵ is selected from H and C₁₋₂-alkyl.

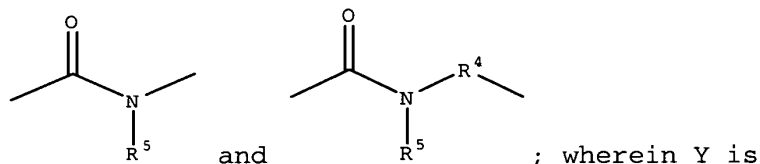
2025 RELEASE UNDER E.O. 14176

7. Compound of Claim 6 wherein A is selected from

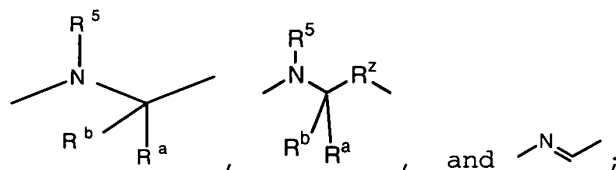


wherein R^c is selected from H, methyl and optionally

5 substituted phenyl; wherein X is selected from



selected from

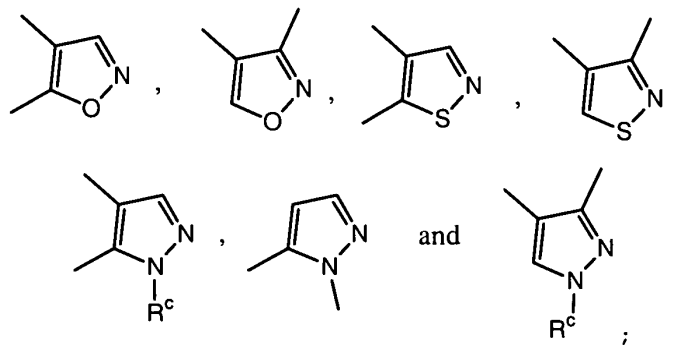


wherein R^a and R^b are independently selected from H, halo,

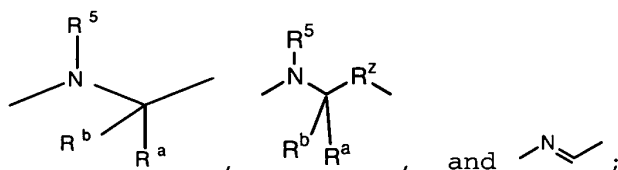
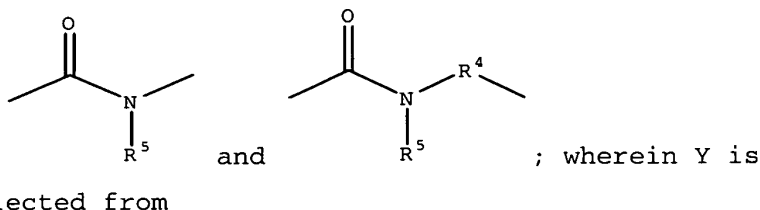
- 10 and C_{1-2} -alkyl; wherein R^z is C_1 - C_2 alkylene; wherein R is selected from substituted or unsubstituted 4-pyridyl, 4-pyrimidinyl, 5-pyrimidinyl, 6-pyrimidinyl, 4-pyridazinyl, 6-pyridazinyl, indazolyl, quinolinyl, isoquinolinyl, quinazolinyl, triazolyl and 4-pyrazolyl; wherein substituted
- 15 R is substituted with one or more substituents independently selected from halo, $-OR^3$, $-SR^3$, $-CO_2R^3$, $-CONR^3R^3$, $-COR^3$, $-NR^3R^3$, $-SO_2NR^3R^3$, $-NR^3C(O)OR^3$, $-NR^3C(O)R^3$, cycloalkyl, optionally substituted 5-6 membered heterocyclyl, optionally substituted phenyl, C_{1-2} -alkyl, cyano, C_{1-2} -hydroxyalkyl,
- 20 nitro and C_{1-2} -haloalkyl; wherein R^1 is a substituted or unsubstituted substituent selected from phenyl, indenyl, thienyl, indolyl, pyridyl, naphthyl, tetrahydronaphthyl, 2,1,3-benzothiadiazolyl, indazolyl, quinolyl, isoquinolyl, pyrimidinyl, pyridazinyl, pyrazolyl, imidazolyl, oxazolyl,
- 25 thiazolyl, thiadiazolyl, tetrahydroquinolinyl,

benzodioxanyl, quinazolinyl, furyl and pyrrolyl; wherein substituted R^1 is substituted with one or more substituents independently selected from halo, $-OR^3$, $-SR^3$, $-CO_2R^3$, $-CONR^3R^3$, $-COR^3$, $-NR^3R^3$, $-NH(C_1-C_2\text{-alkylenyl}-R^3)$, $-(C_1-C_2\text{-alkylenyl})NR^3R^3$, $-SO_2NR^3R^3$, $-NR^3C(O)OR^3$, $-NR^3C(O)R^3$, optionally substituted cycloalkyl, optionally substituted 5-6 membered heterocyclyl, optionally substituted phenyl, optionally substituted phenyl- C_{1-2} -alkylenyl, optionally substituted 5-6 membered heterocyclyl- C_{1-2} -alkylenyl, C_{1-2} -alkyl, cyano, C_{1-2} -hydroxyalkyl, nitro and C_{1-2} -haloalkyl; wherein R^2 is one or more substituents independently selected from H, halo, $-OR^3$, oxo, $-SR^3$, $-CO_2R^3$, $-CONR^3R^3$, $-COR^3$, $-NR^3R^3$, $-SO_2NR^3R^3$, $-NR^3C(O)OR^3$, $-NR^3C(O)R^3$, cycloalkyl, optionally substituted 5-6 membered heterocyclyl, optionally substituted phenyl, C_{1-2} -alkyl, cyano, C_{1-2} -hydroxyalkyl, C_{1-3} -carboxyalkyl, nitro, C_{2-3} -alkenyl, C_{2-3} -alkynyl and C_{1-2} -haloalkyl; wherein R^3 is selected from H, methyl, ethyl, cyclopropyl, cyclohexyl and trifluoromethyl; wherein R^4 is C_{2-3} -alkylenyl; and wherein R^5 is from H, methyl or ethyl; and pharmaceutically acceptable salts thereof.

8. Compound of Claim 6 wherein A is selected from



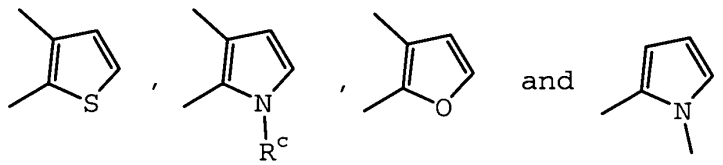
wherein R^c is selected from H, methyl and optionally substituted phenyl; wherein X is selected from



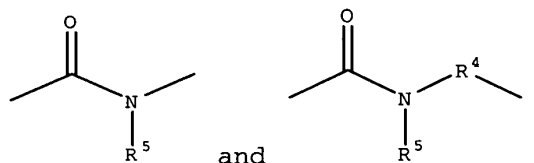
- wherein R^a and R^b are independently selected from H, halo, and C_{1-2} -alkyl; wherein R^z is C_1 - C_2 alkylene; wherein R is selected from substituted or unsubstituted 4-pyridyl, 4-pyrimidinyl, 5-pyrimidinyl, 6-pyrimidinyl, 4-pyridazinyl, 6-pyridazinyl, indazolyl, quinolinyl, isoquinolinyl, quinazolinyl, triazolyl and 4-pyrazolyl; wherein substituted R is substituted with one or more substituents independently selected from halo, $-OR^3$, $-SR^3$, $-CO_2R^3$, $-CONR^3R^3$, $-COR^3$, $-NR^3R^3$, $-SO_2NR^3R^3$, $-NR^3C(O)OR^3$, $-NR^3C(O)R^3$, cycloalkyl, optionally substituted 5-6 membered heterocyclyl, optionally substituted phenyl, C_{1-2} -alkyl, cyano, C_{1-2} -hydroxyalkyl, nitro and C_{1-2} -haloalkyl; wherein R^1 is a substituted or unsubstituted substituent selected from phenyl, indenyl, thienyl, indolyl, pyridyl, naphthyl, tetrahydronaphthyl, 2,1,3-benzothiadiazolyl, indazolyl, quinolyl, isoquinolyl, pyrimidinyl, pyridazinyl, pyrazolyl, imidazolyl, oxazolyl, thiazolyl, thiadiazolyl, tetrahydroquinolinyl, benzodioxanyl, quinazolinyl, furyl and pyrrolyl; wherein substituted R^1 is substituted with one or more substituents independently selected from halo, $-OR^3$, $-SR^3$, $-CO_2R^3$, $-CONR^3R^3$, $-COR^3$, $-NR^3R^3$, $-NH(C_1-C_2-alkylene-R^3)$, $-(C_1-C_2-alkylene)NR^3R^3$, $-SO_2NR^3R^3$, $-NR^3C(O)OR^3$, $-NR^3C(O)R^3$, optionally substituted cycloalkyl, optionally substituted 5-6 membered heterocyclyl, optionally substituted phenyl, optionally substituted phenyl- C_{1-2} -alkylene, optionally substituted 5-6

membered heterocyclyl-C₁-C₂-alkylenyl, C₁₋₂-alkyl, cyano, C₁₋₂-hydroxyalkyl, nitro and C₁₋₂-haloalkyl; wherein R² is one or more substituents independently selected from H, halo, -OR³, oxo, -SR³, -CO₂R³, -CONR³R³, -COR³, -NR³R³, -SO₂NR³R³, -NR³C(O)OR³, -NR³C(O)R³, cycloalkyl, optionally substituted 5-6 membered heterocyclyl, optionally substituted phenyl, C₁₋₂-alkyl, cyano, C₁₋₂-hydroxyalkyl, C₁₋₃-carboxyalkyl, nitro, C₂₋₃-alkenyl, C₂₋₃-alkynyl and C₁₋₂-haloalkyl; wherein R³ is selected from H, methyl, ethyl, cyclopropyl, cyclohexyl and trifluoromethyl; wherein R⁴ is C₂₋₃-alkylenyl; and wherein R⁵ is from H, methyl or ethyl; and pharmaceutically acceptable salts thereof.

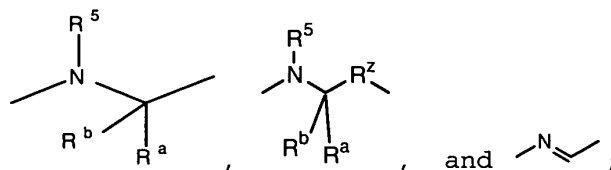
9. Compound of Claim 6 wherein A is selected from



wherein R^c is selected from H, methyl and optionally substituted phenyl; wherein X is selected from



wherein Y is selected from



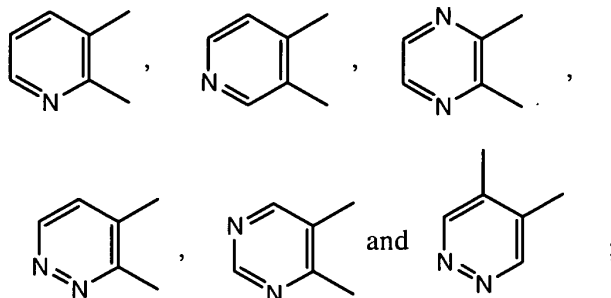
wherein R^a and R^b are independently selected from H, halo, and C₁₋₂-alkyl; wherein R^z is C₁-C₂ alkylenyl; wherein R is selected from substituted or unsubstituted 4-pyridyl, 4-pyrimidinyl, 5-pyrimidinyl, 6-pyrimidinyl, 4-pyridazinyl, 6-

25

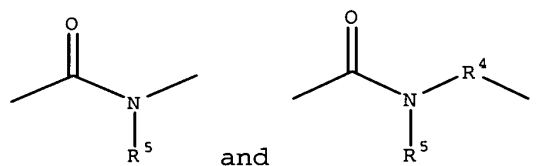
pyridazinyl, indazolyl, quinolinyl, isoquinolinyl, quinazolinyl, triazolyl and 4-pyrazolyl; wherein substituted R is substituted with one or more substituents independently selected from halo, -OR³, -SR³, -CO₂R³, -CONR³R³, -COR³, -NR³R³, -SO₂NR³R³, -NR³C(O)OR³, -NR³C(O)R³, cycloalkyl, optionally substituted 5-6 membered heterocyclyl, optionally substituted phenyl, C₁₋₂-alkyl, cyano, C₁₋₂-hydroxyalkyl, nitro and C₁₋₂-haloalkyl; wherein R¹ is a substituted or unsubstituted substituent selected from phenyl, indenyl, thienyl, indolyl, pyridyl, naphthyl, tetrahydronaphthyl, 2,1,3-benzothiadiazolyl, indazolyl, quinolyl, isoquinolyl, pyrimidinyl, pyridazinyl, pyrazolyl, imidazolyl, oxazolyl, thiazolyl, thiadiazolyl, tetrahydroquinolinyl, benzodioxanyl, quinazolinyl, furyl and pyrrolyl; wherein substituted R¹ is substituted with one or more substituents independently selected from halo, -OR³, -SR³, -CO₂R³, -CONR³R³, -COR³, -NR³R³, -NH(C₁-C₂-alkylenyl-R³), -(C₁-C₂-alkylenyl)NR³R³, -SO₂NR³R³, -NR³C(O)OR³, -NR³C(O)R³, optionally substituted cycloalkyl, optionally substituted 5-6 membered heterocyclyl, optionally substituted phenyl, optionally substituted phenyl-C₁₋₂-alkylenyl, optionally substituted 5-6 membered heterocyclyl-C₁-C₂-alkylenyl, C₁₋₂-alkyl, cyano, C₁₋₂-hydroxyalkyl, nitro and C₁₋₂-haloalkyl; wherein R² is one or more substituents independently selected from H, halo, -OR³, oxo, -SR³, -CO₂R³, -CONR³R³, -COR³, -NR³R³, -SO₂NR³R³, -NR³C(O)OR³, -NR³C(O)R³, cycloalkyl, optionally substituted 5-6 membered heterocyclyl, optionally substituted phenyl, C₁₋₂-alkyl, cyano, C₁₋₂-hydroxyalkyl, C₁₋₃-carboxyalkyl, nitro, C₂₋₃-alkenyl, C₂₋₃-alkynyl and C₁₋₂-haloalkyl; wherein R³ is selected from H, methyl, ethyl, cyclopropyl, cyclohexyl and trifluoromethyl; wherein R⁴ is C₂₋₃-alkylenyl; and wherein R⁵ is from H, methyl or ethyl; and pharmaceutically acceptable salts thereof.

2004584 044003

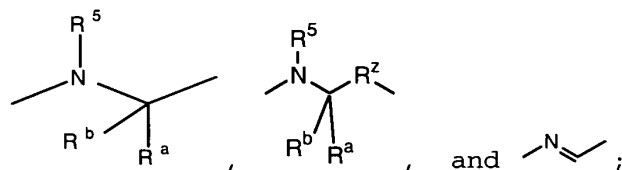
10. Compound of Claim 1, and pharmaceutically acceptable salts thereof, wherein A is selected from



5 wherein X is selected from



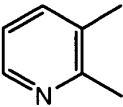
wherein Y is selected from

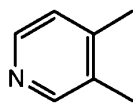


10 wherein R^a and R^b are independently selected from H, halo, and C₁₋₂-alkyl; wherein R² is C₁-C₂ alkylene; wherein R is selected from substituted or unsubstituted 4-pyridyl, 4-pyrimidinyl, 5-pyrimidinyl, 6-pyrimidinyl, 4-pyridazinyl, 6-pyridazinyl, indazolyl, quinolinyl, isoquinolinyl, quinazolinyl, triazolyl and 4-pyrazolyl; wherein substituted
 15 R is substituted with one or more substituents independently selected from halo, -OR³, -SR³, -CO₂R³, -CONR³R³, -COR³, -NR³R³, -SO₂NR³R³, -NR³C(O)OR³, -NR³C(O)R³, cycloalkyl, optionally substituted 5-6 membered heterocyclyl, optionally substituted phenyl, C₁₋₂-alkyl, cyano, C₁₋₂-hydroxyalkyl,
 20 nitro and C₁₋₂-haloalkyl; wherein R¹ is a substituted or unsubstituted substituent group selected from phenyl, indenyl, thienyl, indolyl, pyridyl, naphthyl,

tetrahydronaphthyl, 2,1,3-benzothiadiazolyl, indazolyl,
 quinolyl, isoquinolyl, pyrimidinyl, pyridazinyl, pyrazolyl,
 imidazolyl, oxazolyl, thiazolyl, thiadiazolyl,
 tetrahydroquinolinyl, benzodioxanyl, quinazolinyl, furyl and
 5 pyrrolyl; wherein substituted R^1 is substituted with one or
 more substituents independently selected from halo, $-OR^3$, $-$
 SR^3 , $-CO_2R^3$, $-CONR^3R^3$, $-COR^3$, $-NR^3R^3$, $-NH(C_1-C_2\text{-alkylenyl}-R^3)$, $-$
 $(C_1-C_2\text{-alkylenyl})NR^3R^3$, $-SO_2NR^3R^3$, $-NR^3C(O)OR^3$, $-NR^3C(O)R^3$,
 optionally substituted cycloalkyl, optionally substituted 5-
 10 6 membered heterocyclyl, optionally substituted phenyl,
 optionally substituted phenyl- C_{1-2} -alkylenyl, optionally
 substituted 5-6 membered heterocyclyl- C_1-C_2 -alkylenyl, C_{1-2} -
 alkyl, cyano, C_{1-2} -hydroxyalkyl, nitro and C_{1-2} -haloalkyl;
 wherein R^2 is one or more substituents independently
 15 selected from H, halo, $-OR^3$, oxo, $-SR^3$, $-CO_2R^3$, $-CONR^3R^3$, $-$
 COR^3 , $-NR^3R^3$, $-SO_2NR^3R^3$, $-NR^3C(O)OR^3$, $-NR^3C(O)R^3$, cycloalkyl,
 optionally substituted 5-6 membered heterocyclyl, optionally
 substituted phenyl, C_{1-2} -alkyl, cyano, C_{1-2} -hydroxyalkyl, C_{1-3} -
 carboxyalkyl, nitro, C_{2-3} -alkenyl, C_{2-3} -alkynyl and C_{1-2} -
 20 haloalkyl; wherein R^3 is selected from H, methyl, ethyl,
 cyclopropyl, cyclohexyl and trifluoromethyl; wherein R^4 is
 C_{2-3} -alkylenyl; and wherein R^5 is from H, methyl or ethyl;
 and pharmaceutically acceptable salts thereof.

25 11. Compound of Claim 10, and pharmaceutically

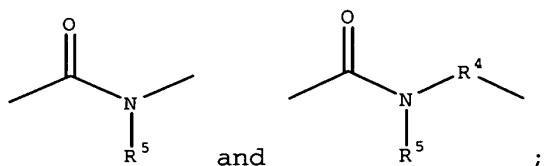
acceptable salts thereof, wherein A is , or



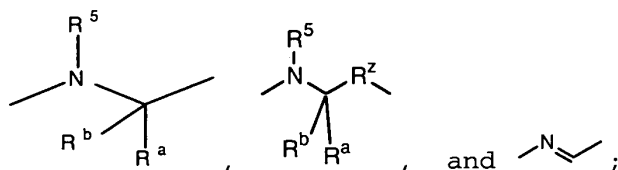
; wherein X is $-C(O)-NH-$; wherein Y is $-NH-CH_2-$;
 wherein R is selected from substituted or unsubstituted 4-
 pyridyl, 4-quinolyl, 5-quinolyl, 6-quinolyl, 4-isoquinolyl,
 30 5-isoquinolyl, 6-isoquinolyl, 5-indazolyl, 4-pyrimidinyl and

4-pyridazinyl; wherein substituted R is substituted with one or more substituents independently selected from halo, -OR³, -SR³, -CO₂R³, -CONR³R³, -COR³, -NR³R³, -SO₂NR³R³, -NR³C(O)OR³, -NR³C(O)R³, cycloalkyl, optionally substituted 5-6 membered heterocyclyl, optionally substituted phenyl, C₁₋₂-alkyl, cyano, C₁₋₂-hydroxyalkyl, nitro and C₁₋₂-haloalkyl; wherein R¹ is selected from substituted or unsubstituted phenyl, indazolyl, indolyl, 2,1,3-benzothiadiazolyl, isoquinolyl, quinolyl, tetrahydroquinolyl, benzodioxanyl, and quinazolinyl; wherein substituted R¹ is substituted with one or more substituents independently selected from halo, -OR³, -SR³, -CO₂R³, -CONR³R³, -COR³, -NR³R³, -SO₂NR³R³, -NR³C(O)OR³, -NR³C(O)R³, optionally substituted cycloalkyl, optionally substituted 5-6 membered heterocyclyl, optionally substituted phenyl, optionally substituted phenyl-C₁₋₂-alkylenyl, morpholinylmethyl, methylpiperidinylmethyl, methylpiperazinylmethyl, C₁₋₂-alkyl, cyano, C₁₋₂-hydroxyalkyl, nitro and C₁₋₂-haloalkyl; wherein R² is one or more substituents independently selected from H, halo, -OR³, oxo, -SR³, -CO₂R³, -CONR³R³, -COR³, -NR³R³, -SO₂NR³R³, -NR³C(O)OR³, -NR³C(O)R³, cycloalkyl, optionally substituted 5-6 membered heterocyclyl, optionally substituted phenyl, C₁₋₂-alkyl, cyano, C₁₋₂-hydroxyalkyl, C₁₋₃-carboxyalkyl, nitro, C₂₋₃-alkenyl, C₂₋₃-alkynyl and C₁₋₂-haloalkyl; wherein R³ is selected from H, methyl, ethyl, cyclopropyl, cyclohexyl and trifluoromethyl; wherein R⁴ is C₂₋₃-alkylenyl; and wherein R⁵ is from H, methyl or ethyl.

12. Compound of Claim 1 wherein A is 9- or 10-membered fused partially saturated heterocyclyl or 9- or 10-membered fused heteroaryl; wherein X is selected from



wherein Y is selected from



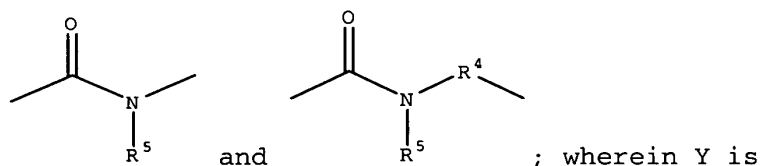
- wherein R^a and R^b are independently selected from H, halo, cyano, and C_{1-2} -alkyl substituted with R^2 , or wherein R^a and R^b together form C_3-C_4 cycloalkyl; wherein R^Z is C_1-C_2 alkylene, where one of the CH_2 groups may be substituted with an oxygen atom or an $-NH-$; wherein R is selected from substituted or unsubstituted 5-6 membered heteroaryl comprising one or more nitrogen atoms, and substituted or unsubstituted 9-10 membered fused heteroaryl comprising one or more nitrogen atoms; wherein substituted R is substituted with one or more substituents independently selected from halo, $-OR^3$, $-SR^3$, $-CO_2R^3$, $-CONR^3R^3$, $-COR^3$, $-NR^3R^3$, $-SO_2NR^3R^3$, $-NR^3C(O)OR^3$, $-NR^3C(O)R^3$, cycloalkyl, optionally substituted 5-6 membered heterocyclyl, optionally substituted phenyl, C_{1-2} -alkyl, cyano, C_{1-2} -hydroxyalkyl, nitro and C_{1-2} -haloalkyl; wherein R^1 is selected from substituted or unsubstituted aryl selected from phenyl, naphthyl, indenyl and tetrahydronaphthyl, substituted or unsubstituted 5-6 membered heteroaryl, and substituted or unsubstituted 9-10 membered fused heteroaryl; wherein substituted R^1 is substituted with one or more substituents independently selected from halo, $-OR^3$, $-SR^3$, $-SO_2R^3$, $-CO_2R^3$, $-CONR^3R^3$, $-COR^3$, $-NR^3R^3$, $-NH(C_{1-2} \text{ alkylene}R^3)$, $-(C_{1-2} \text{ alkylene})NR^3R^3$, $-SO_2NR^3R^3$, $-NR^3C(O)OR^3$, $-NR^3C(O)R^3$, optionally substituted cycloalkyl, optionally substituted 5-6 membered heterocyclyl, optionally substituted phenyl, optionally

substituted phenyl-C₁₋₂-alkylenyl, optionally substituted 5-6
 membered heterocyclyl-C₁₋₂-alkylenyl, C₁₋₂-alkyl, cyano, C₁₋₂-
 hydroxyalkyl, nitro and C₁₋₂-haloalkyl; wherein R² is one or
 more substituents independently selected from H, halo, -OR³,
 5 oxo, -SR³, -CO₂R³, -CONR³R³, -COR³, -NR³R³, -SO₂NR³R³, -
 NR³C(O)OR³, -NR³C(O)R³, cycloalkyl, optionally substituted 5-
 6 membered heterocyclyl, optionally substituted phenyl, C₁₋₂-
 alkyl, cyano, C₁₋₂-hydroxyalkyl, C₁₋₃-carboxyalkyl, nitro, C₂₋₃-
 alkenyl, C₂₋₃-alkynyl and C₁₋₂-haloalkyl; wherein R³ is
 10 selected from H, C₁₋₂-alkyl, phenyl, C₃₋₆ cycloalkyl and C₁₋₂-
 haloalkyl; wherein R⁴ is C₂₋₃-alkylenyl, where one of the CH₂
 groups may be substituted with an oxygen atom or an -NH-;
 and wherein R⁵ is selected from H and C₁₋₂-alkyl; and
 pharmaceutically acceptable salts thereof.

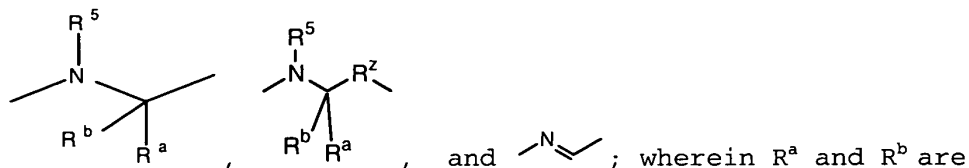
15

13. Compound of Claim 12 wherein A is selected from
 benzothienyl, benzofuryl, benzimidazolyl, benzoxazolyl,
 benzthiazolyl, indazolyl, indolyl, isoindolyl, quinolyl,
 isoquinolyl, naphthpyridinyl, tetrahydroquinolyl,
 20 quinoxalinyl and quinazolinyl;
 and pharmaceutically acceptable salts thereof.

14. Compound of Claim 1, and pharmaceutically
 acceptable salts thereof, wherein A is 5- or 6-membered
 25 cycloalkenyl; wherein X is selected from



selected from



- independently selected from H, halo, cyano, and C_{1-2} -alkyl substituted with R^2 , or wherein R^a and R^b together form $\text{C}_3\text{-C}_4$ cycloalkyl; wherein R^z is $\text{C}_1\text{-C}_2$ alkylene, where one of the CH_2 groups may be substituted with an oxygen atom or an -NH- ; wherein R is selected from substituted or unsubstituted 5-6 membered heteroaryl comprising one or more nitrogen atoms, and substituted or unsubstituted 9-10 membered fused heteroaryl comprising one or more nitrogen atoms; wherein substituted R is substituted with one or more substituents independently selected from halo, -OR^3 , -SR^3 , $\text{-CO}_2\text{R}^3$, $\text{-CONR}^3\text{R}^3$, -COR^3 , $\text{-NR}^3\text{R}^3$, $\text{-SO}_2\text{NR}^3\text{R}^3$, $\text{-NR}^3\text{C}(\text{O})\text{OR}^3$, $\text{-NR}^3\text{C}(\text{O})\text{R}^3$, cycloalkyl, optionally substituted 5-6 membered heterocyclyl, optionally substituted phenyl, C_{1-2} -alkyl, cyano, C_{1-2} -hydroxyalkyl, nitro and C_{1-2} -haloalkyl; wherein R^1 is selected from substituted or unsubstituted aryl selected from phenyl, naphthyl, indenyl and tetrahydronaphthyl, substituted or unsubstituted 5-6 membered heteroaryl, and substituted or unsubstituted 9-10 membered fused heteroaryl; wherein substituted R^1 is substituted with one or more substituents independently selected from halo, -OR^3 , -SR^3 , $\text{-SO}_2\text{R}^3$, $\text{-CO}_2\text{R}^3$, $\text{-CONR}^3\text{R}^3$, -COR^3 , $\text{-NR}^3\text{R}^3$, $\text{-NH}(\text{C}_{1-2} \text{ alkylene} \text{R}^3)$, $\text{-(C}_{1-2} \text{ alkylene})\text{NR}^3\text{R}^3$, $\text{-SO}_2\text{NR}^3\text{R}^3$, $\text{-NR}^3\text{C}(\text{O})\text{OR}^3$, $\text{-NR}^3\text{C}(\text{O})\text{R}^3$, optionally substituted cycloalkyl, optionally substituted 5-6 membered heterocyclyl, optionally substituted phenyl, optionally substituted phenyl- C_{1-2} -alkylene, optionally substituted 5-6 membered heterocyclyl- C_{1-2} -alkylene, C_{1-2} -alkyl, cyano, C_{1-2} -hydroxyalkyl, nitro and C_{1-2} -haloalkyl; wherein R^2 is one or more substituents independently selected from H, halo, -OR^3 , oxo, -SR^3 , $\text{-CO}_2\text{R}^3$, $\text{-CONR}^3\text{R}^3$, -COR^3 , $\text{-NR}^3\text{R}^3$, $\text{-SO}_2\text{NR}^3\text{R}^3$, -

NR³C(O)OR³, -NR³C(O)R³, cycloalkyl, optionally substituted 5-6 membered heterocyclyl, optionally substituted phenyl, C₁₋₂-alkyl, cyano, C₁₋₂-hydroxyalkyl, C₁₋₃-carboxyalkyl, nitro, C₂₋₃-alkenyl, C₂₋₃-alkynyl and C₁₋₂-haloalkyl; wherein R³ is
5 selected from H, C₁₋₂-alkyl, phenyl, C₃₋₆ cycloalkyl and C₁₋₂-haloalkyl; wherein R⁴ is C₂₋₃-alkylenyl, where one of the CH₂ groups may be substituted with an oxygen atom or an -NH-; and wherein R⁵ is selected from H and C₁₋₂-alkyl.

10 15. Compound of Claim 14 wherein A is cyclopentadienyl or cyclopentenyl; and pharmaceutically acceptable salts thereof.

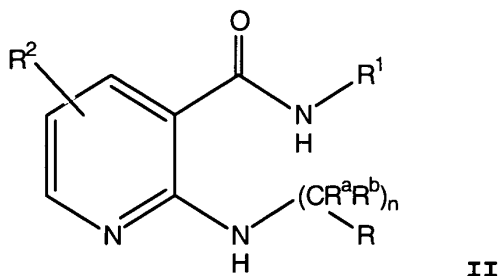
15 16. Compound of Claim 1 and pharmaceutically acceptable salts thereof selected from
N-(4-chlorophenyl)-3-[(4-pyridinylmethylene)amino]-4-pyridinecarboxamide;
N-(4-chlorophenyl){3-[(4-pyridylmethyl)amino](2-thienyl)}carboxamide;
20 N-phenyl{3-[(4-pyridylmethyl)amino](2-thienyl)}carboxamide;
N-(4-chlorophenyl){2-[(4-pyridylmethyl)amino](3-pyridyl)}carboxamide;
N-(3,4-dichlorophenyl){2-[(4-pyridylmethyl)amino](3-pyridyl)}carboxamide;
25 N-(3-chlorophenyl){2-[(4-pyridylmethyl)amino](3-pyridyl)}carboxamide;
N-(4-chlorophenyl){3-[(4-pyridylmethyl)amino](2-pyridyl)}carboxamide;
N-(4-chlorophenyl){3-[(6-quinolylmethyl)amino](2-pyridyl)}carboxamide;
30 N-(3,4-dichlorophenyl){2-[(6-quinolylmethyl)amino](3-pyridyl)}carboxamide;
N-(4-chlorophenyl){6-methyl-2-[(4-pyridylmethyl)amino](3-pyridyl)}carboxamide;

546/

- N-(3,4-dichlorophenyl){6-methyl-2-[(4-pyridylmethyl)amino](3-pyridyl)}carboxamide;
N-(3-fluoro-4-methylphenyl){6-methyl-2-[(4-pyridylmethyl)amino](3-pyridyl)}carboxamide;
5 N-(3,4-dichlorophenyl){6-chloro-2-[(4-pyridylmethyl)amino](3-pyridyl)}carboxamide;
N-(4-chlorophenyl){6-chloro-2-[(4-pyridylmethyl)amino](3-pyridyl)}carboxamide;
{6-chloro-2-[(4-pyridylmethyl)amino](3-pyridyl)}-N-(3-
10 fluorophenyl)carboxamide;
N-(3-chlorophenyl){6-chloro-2-[(4-pyridylmethyl)amino](3-pyridyl)}carboxamide;
N-(4-chlorophenyl){3-[(4-pyridylmethyl)amino](4-pyridyl)}carboxamide;
15 N-(3-fluoro-4-methylphenyl){2-[(4-pyridylmethyl)amino](3-pyridyl)}carboxamide;
N-(4-chlorophenyl){2-[(4-quinolylmethyl)amino](3-pyridyl)}carboxamide;
N-(4-chlorophenyl){2-[(5-quinolylmethyl)amino](3-pyridyl)}carboxamide;
20 N-(4-chlorophenyl){2-[(4-pyridylethyl)amino]-5-(3-thienyl)-(3-pyridyl)}carboxamide;
N-(4-chlorophenyl){5-(4-methoxyphenyl)-2-[(4-pyridylmethyl)amino]-(3-pyridyl)}carboxamide; and
25 N-(4-chlorophenyl){5-bromo-2-[(4-pyridylmethyl)amino]-(3-pyridyl)}carboxamide.

17. A compound of Claim 1 having Formula II

2004581-01001
"01001" 1894001



wherein R^a and R^b are independently selected from H, halo,
C₁₋₄-alkyl and -N(R⁶)₂;

5 wherein n is 1-2;

wherein R is selected from

a) unsubstituted or substituted 5- or 6-membered
nitrogen-containing heteroaryl, and

b) unsubstituted or substituted 9- or 10-membered
10 fused nitrogen-containing heteroaryl,

where R is substituted with one or more substituents
selected from halo, amino, hydroxy, C₁₋₆-alkyl, C₁₋₆-
6-haloalkyl and C₁₋₆-alkoxy;

wherein R¹ is selected from unsubstituted or substituted
15 aryl,

5-6 membered heteroaryl and

9-10 membered fused heteroaryl,

wherein substituted R¹ is substituted with one or more
substituents selected from halo, C₁₋₆-alkyl, optionally
20 substituted C₃₋₆-cycloalkyl, optionally substituted
phenyl, C₁₋₆-haloalkoxy, optionally substituted
phenyloxy, benzyl, optionally substituted 5-6 membered
heterocyclyl-C₁-C₂-alkylenyl, optionally substituted
heteroaryl, optionally substituted heteroaryloxy, C₁₋₆-
25 haloalkyl, and C₁₋₆-alkoxy;

wherein R² is one or more substituents independently
selected from

H,

halo,

C₁₋₆-alkyl,
C₁₋₆-haloalkyl,
C₁₋₆-alkoxy,
C₁₋₆-haloalkoxy,
5 C₁₋₆-carboxyalkyl,
unsubstituted or substituted aryl and
unsubstituted or substituted 5-6 membered
heteroaryl; and
wherein R⁶ is H or C₁₋₆-alkyl;
10 and pharmaceutically acceptable isomers and salts thereof.

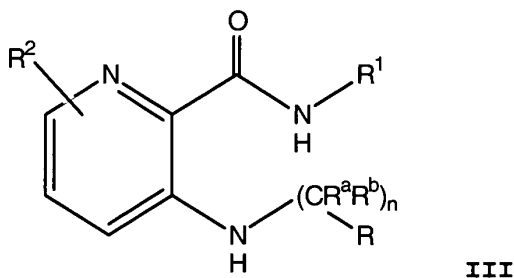
18. Compound of Claim 17 wherein R^a and R^b are H;
wherein n is 1-2;
wherein R is selected from 4-pyridyl, pyrimidinyl,
15 triazolyl, pyridazinyl, indolyl, isoindolyl,
indazolyl, quinolyl, isoquinolyl, naphthyridinyl and
quinoxalinyl, where R is unsubstituted or substituted
with one or more substituents selected
from chloro, fluoro, amino, hydroxy, methyl, ethyl,
20 propyl, trifluoromethyl, methoxy and ethoxy;
wherein R¹ is selected from phenyl, tetrahydronaphthyl,
naphthyl, isoquinolyl, quinolyl, pyridyl, pyrimidinyl,
pyridazinyl, indolyl, isoindolyl, naphthyridinyl,
quinoxalinyl, tetrahydroquinolinyl, indazolyl,
25 benzothienyl, benzofuryl, benzimidazolyl,
benzoxazolyl, or benzthiazolyl, where R¹ is
unsubstituted or substituted with one or more
substituents selected
from chloro, fluoro, amino, hydroxy, cyclohexyl,
30 phenylmethyl, morpholinylmethyl,
methylpiperidinylmethyl, methylpiperazinylmethyl,
ethyl, propyl, trifluoromethyl, phenyloxy,
methoxy and ethoxy; and

401855-0100
2007-03-20

wherein R² is one or more substituents independently
selected from H, chloro, fluoro, bromo, amino,
hydroxy, methyl, ethyl, propyl, trifluoromethyl,
methoxy, ethoxy, trifluoromethoxy, carboxymethyl,
5 unsubstituted or substituted phenyl and unsubstituted
or substituted heteroaryl selected
from thienyl, furanyl, pyridyl, imidazolyl, and
pyrazolyl;
and pharmaceutically acceptable salts thereof.

10

19. A compound of Claim 1 having Formula III



- 15 wherein R^a and R^b are independently selected from H, halo,
C₁₋₄-alkyl and -N(R⁶)₂;
wherein n is 1-2;
wherein R is selected from
a) unsubstituted or substituted 5- or 6-membered
20 nitrogen-containing heteroaryl, and
b) unsubstituted or substituted 9- or 10-membered
fused nitrogen-containing heteroaryl,
where R is substituted with one or more substituents
selected from halo, amino, hydroxy, C₁₋₆-alkyl, C₁₋₆-
25 haloalkyl and C₁₋₆-alkoxy;
wherein R¹ is selected from unsubstituted or substituted
aryl,
5-6 membered heteroaryl and
9-10 membered fused heteroaryl,

wherein substituted R¹ is substituted with one or more
substituents selected from halo, C₁₋₆-alkyl, optionally
substituted C₃₋₆-cycloalkyl, optionally substituted
phenyl, optionally substituted 5-6 membered
5 heterocyclyl-C₁-C₂-alkylenyl, C₁₋₆-haloalkoxy,
optionally substituted phenyloxy, benzyl, optionally
substituted heteroaryl, optionally substituted
heteroaryloxy, C₁₋₆-haloalkyl, and C₁₋₆-alkoxy;

wherein R² is one or more substituents independently
10 selected from

H,
halo,
C₁₋₆-alkyl,
C₁₋₆-haloalkyl,
15 C₁₋₆-alkoxy,
C₁₋₆-haloalkoxy,
C₁₋₆-carboxyalkyl,
unsubstituted or substituted aryl and
unsubstituted or substituted 5-6 membered
20 heteroaryl; and

wherein R⁶ is H or C₁₋₆-alkyl;

and pharmaceutically acceptable isomers and salts thereof.

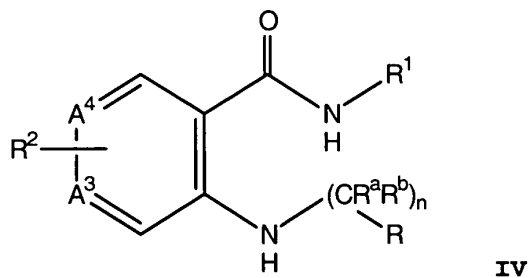
20. Compound of Claim 19 wherein R^a and R^b are H;

25 wherein n is 1-2;

wherein R is selected from 4-pyridyl, pyrimidinyl,
pyridazinyl, indolyl, isoindolyl, indazolyl, quinolyl,
isoquinolyl, naphthyridinyl and quinoxalyl, where R
is unsubstituted or substituted with one or more
30 substituents selected
from chloro, fluoro, amino, hydroxy, methyl, ethyl,
propyl, trifluoromethyl, methoxy and ethoxy;
wherein R¹ is selected from phenyl, tetrahydronaphthyl,
naphthyl, isoquinolyl, quinolyl, pyridyl, pyrimidinyl,

- pyridazinyl, indolyl, isoindolyl, naphthyridinyl,
 quinoxalinyl, tetrahydroquinolinyl, indazolyl,
 benzothienyl, benzofuryl, benzimidazolyl,
 benzoxazolyl, or benzthiazolyl, where R¹ is
 5 unsubstituted or substituted with one or more
 substituents selected
 from chloro, fluoro, amino, hydroxy, cyclohexyl,
 phenylmethyl, morpholinylmethyl,
 methylpiperdinylmethyl, methylpiperazinylmethyl,
 10 ethyl, propyl, trifluoromethyl, phenyloxy,
 methoxy and ethoxy; and
 wherein R² is one or more substituents independently
 selected from H, chloro, fluoro, bromo, amino,
 hydroxy, methyl, ethyl, propyl, trifluoromethyl,
 15 methoxy, ethoxy, trifluoromethoxy, carboxymethyl,
 unsubstituted or substituted phenyl and unsubstituted
 or substituted heteroaryl selected
 from thienyl, furanyl, pyridyl, imidazolyl, and
 pyrazolyl;
 20 and pharmaceutically acceptable salts thereof.

21. A compound of Claim 1 having Formula IV



- 25 wherein A³ is selected from CR² and N;
 wherein A⁴ is selected from CR² and N; provided one of A³ and
 A⁴ is not CR²;

wherein R^a and R^b are independently selected from H, halo,
C₁₋₄-alkyl and -N(R⁶)₂;

wherein n is 1-2;

wherein R is selected from

- 5 a) unsubstituted or substituted 5- or 6-membered
 nitrogen-containing heteroaryl, and
 b) unsubstituted or substituted 9- or 10-membered
 fused nitrogen-containing heteroaryl,
 where R is substituted with one or more substituents
10 selected from halo, amino, hydroxy, C₁₋₆-alkyl, C₁₋₆-haloalkyl and C₁₋₆-alkoxy;

wherein R¹ is selected from unsubstituted or substituted
aryl,

- 5-6 membered heteroaryl and
15 9-10 membered fused heteroaryl,

wherein substituted R¹ is substituted with one or more
substituents selected from halo, C₁₋₆-alkyl, optionally
substituted C₃₋₆-cycloalkyl, optionally substituted
phenyl, optionally substituted 5-6 membered
20 heterocyclyl-C₁-C₂-alkylenyl, C₁₋₆-haloalkoxy,
 optionally substituted phenyloxy, benzyl, optionally
 substituted heteroaryl, optionally substituted
 heteroaryloxy, C₁₋₆-haloalkyl, and C₁₋₆-alkoxy;

- wherein R² is one or more substituents independently
25 selected from

- H,
 halo,
 C₁₋₆-alkyl,
 C₁₋₆-haloalkyl,
30 C₁₋₆-alkoxy,
 C₁₋₆-haloalkoxy,
 C₁₋₆-carboxyalkyl,
 unsubstituted or substituted aryl and

1045540

wherein R⁶ is H or C₁₋₆-alkyl;
and pharmaceutically acceptable isomers and salts thereof.

5

wherein R is selected from 4-pyridyl, pyrimidinyl, pyridazinyl, indolyl, isoindolyl, indazolyl, quinolyl, isoquinolyl, naphthyridinyl and quinoxaliny, where R is unsubstituted or substituted with one or more substituents selected from chloro, fluoro, amino, hydroxy, methyl, ethyl, propyl, trifluoromethyl, methoxy and ethoxy;

10

15 wherein R¹ is selected from phenyl, tetrahydronaphthyl,
naphthyl, isoquinolyl, quinolyl, pyridyl, pyrimidinyl,
pyridazinyl, indolyl, isoindolyl, naphthyridinyl,
quinoxaliny, tetrahydroquinoliny, indazolyl,
benzothienyl, benzofuryl, benzimidazolyl,
20 benzoxazolyl, or benzthiazolyl, where R¹ is
unsubstituted or substituted with one or more
substituents selected
from chloro, fluoro, amino, hydroxy, cyclohexyl,
phenylmethyl, morpholinylmethyl,
25 methylpiperidinylmethyl, methylpiperazinylmethyl,
ethyl, propyl, trifluoromethyl, phenyloxy,
methoxy and ethoxy; and

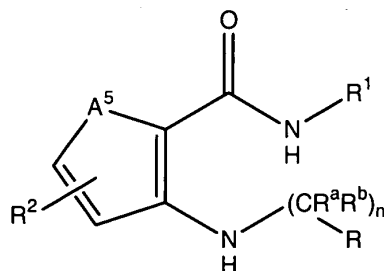
25

wherein R² is one or more substituents independently
selected from H, chloro, fluoro, bromo, amino,
30 hydroxy, methyl, ethyl, propyl, trifluoromethyl,
methoxy, ethoxy, trifluoromethoxy, carboxymethyl,
unsubstituted or substituted phenyl and unsubstituted
or substituted heteroaryl selected

30

from thienyl, furanyl, pyridyl, imidazolyl, and
pyrazolyl;
and pharmaceutically acceptable salts thereof.

5 23. A compound of Claim 1 having the formula V



V

wherein A⁵ is selected from S, O and NR⁶;

10 wherein R^a and R^b are independently selected from H, halo,
C₁₋₄-alkyl and -N(R⁶)₂;

wherein n is 1-2;

wherein R is selected from

15 a) unsubstituted or substituted 5- or 6-membered
nitrogen-containing heteroaryl, and

b) unsubstituted or substituted 9- or 10-membered
fused nitrogen-containing heteroaryl,

20 where R is substituted with one or more substituents
selected from halo, amino, hydroxy, C₁₋₆-alkyl, C₁₋₆-
haloalkyl and C₁₋₆-alkoxy;

wherein R¹ is selected from unsubstituted or substituted
aryl,

5-6 membered heteroaryl and

9-10 membered fused heteroaryl,

25 wherein substituted R¹ is substituted with one or more
substituents selected from halo, C₁₋₆-alkyl, optionally
substituted C₃₋₆-cycloalkyl, optionally substituted
phenyl, C₁₋₆-haloalkoxy, optionally substituted
phenyloxy, benzyl, optionally substituted 5-6 membered

heterocyclyl-C₁-C₂-alkylenyl, optionally substituted heteroaryl, optionally substituted heteroaryloxy, C₁₋₆-haloalkyl, and C₁₋₆-alkoxy;

wherein R² is one or more substituents independently

5 selected from

H,

halo,

C₁₋₆-alkyl,

C₁₋₆-haloalkyl,

10 C₁₋₆-alkoxy,

C₁₋₆-haloalkoxy,

C₁₋₆-carboxyalkyl,

unsubstituted or substituted aryl and

unsubstituted or substituted 5-6 membered

15 heteroaryl; and

wherein R⁶ is H or C₁₋₆-alkyl;

and pharmaceutically acceptable isomers and salts thereof.

24. Compound of Claim 23 wherein R^a and R^b are H;

20 wherein n is 1-2;

wherein R is selected from 4-pyridyl, pyrimidinyl,

pyridazinyl, indolyl, isoindolyl, indazolyl, quinolyl,

isoquinolyl, naphthyridinyl and quinoxaliny, where R

is unsubstituted or substituted with one or more

25 substituents selected

from chloro, fluoro, amino, hydroxy, methyl, ethyl,

propyl, trifluoromethyl, methoxy and ethoxy;

wherein R¹ is selected from phenyl, tetrahydronaphthyl,

naphthyl, isoquinolyl, quinolyl, pyridyl, pyrimidinyl,

30 pyridazinyl, indolyl, isoindolyl, naphthyridinyl,

quinoxaliny, tetrahydroquinoliny, indazolyl,

benzothienyl, benzofuryl, benzimidazolyl,

benzoxazolyl, or benzthiazolyl, where R¹ is

unsubstituted or substituted with one or more
substituents selected

from chloro, fluoro, amino, hydroxy, cyclohexyl,
phenylmethyl, morpholinylmethyl,

5 methylpiperidinylmethyl, methylpiperazinylmethyl,
ethyl, propyl, trifluoromethyl, phenyloxy,
methoxy and ethoxy; and

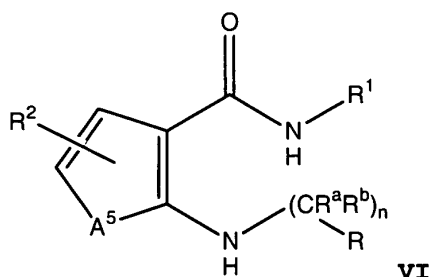
wherein R^2 is one or more substituents independently
selected from H, chloro, fluoro, bromo, amino,

10 hydroxy, methyl, ethyl, propyl, trifluoromethyl,
methoxy, ethoxy, trifluoromethoxy, carboxymethyl,
unsubstituted or substituted phenyl and unsubstituted
or substituted heteroaryl selected

15 from thienyl, furanyl, pyridyl, imidazolyl, and
pyrazolyl;

and pharmaceutically acceptable salts thereof.

25. A compound of Claim 1 having the formula



20 wherein A^5 is selected from S, O and NR^6 ;

wherein R^a and R^b are independently selected from H, halo,
 C_{1-4} -alkyl and $-N(R^6)_2$;

25 wherein n is 1-2;

wherein R is selected from

a) unsubstituted or substituted 5- or 6-membered
nitrogen-containing heteroaryl, and

- b) unsubstituted or substituted 9- or 10-membered fused nitrogen-containing heteroaryl,
where R is substituted with one or more substituents selected from halo, amino, hydroxy, C₁₋₆-alkyl, C₁₋₆-haloalkyl and C₁₋₆-alkoxy;
5 wherein R¹ is selected from unsubstituted or substituted aryl,
5-6 membered heteroaryl and
9-10 membered fused heteroaryl,
10 wherein substituted R¹ is substituted with one or more substituents selected from halo, C₁₋₆-alkyl, optionally substituted C₃₋₆-cycloalkyl, optionally substituted phenyl, C₁₋₆-haloalkoxy, optionally substituted phenyloxy, benzyl, optionally substituted 5-6 membered
15 heterocyclyl-C₁-C₂-alkylenyl, optionally substituted heteroaryl, optionally substituted heteroaryloxy, C₁₋₆-haloalkyl, and C₁₋₆-alkoxy;
wherein R² is one or more substituents independently selected from
20 H,
halo,
C₁₋₆-alkyl,
C₁₋₆-haloalkyl,
C₁₋₆-alkoxy,
25 C₁₋₆-haloalkoxy,
C₁₋₆-carboxyalkyl,
unsubstituted or substituted aryl and
unsubstituted or substituted 5-6 membered heteroaryl; and
30 wherein R⁶ is H or C₁₋₆-alkyl;
and pharmaceutically acceptable isomers and salts thereof.

26. Compound of Claim 25 wherein R^a and R^b are H;
wherein n is 1-2;

wherein R is selected from 4-pyridyl, pyrimidinyl,
pyridazinyl, indolyl, isoindolyl, indazolyl, quinolyl,
isoquinolyl, naphthyridinyl and quinoxalinyl, where R
is unsubstituted or substituted with one or more
5 substituents selected

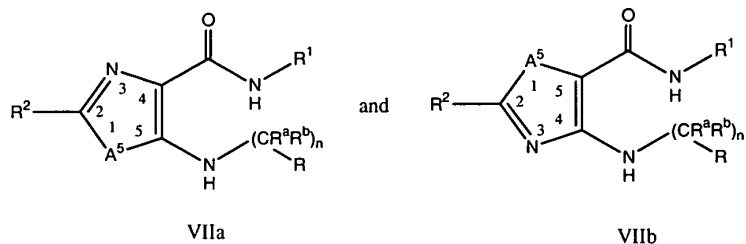
from chloro, fluoro, amino, hydroxy, methyl, ethyl,
propyl, trifluoromethyl, methoxy and ethoxy;
wherein R¹ is selected from phenyl, tetrahydronaphthyl,
naphthyl, isoquinolyl, quinolyl, pyridyl, pyrimidinyl,
10 pyridazinyl, indolyl, isoindolyl, naphthyridinyl,
quinoxalinyl, tetrahydroquinolyl, indazolyl,
benzothienyl, benzofuryl, benzimidazolyl,
benzoxazolyl, or benzthiazolyl, where R¹ is
unsubstituted or substituted with one or more
15 substituents selected

from chloro, fluoro, amino, hydroxy, cyclohexyl,
phenylmethyl, morpholinylmethyl,
methylpiperidinylmethyl, methylpiperazinylmethyl,
ethyl, propyl, trifluoromethyl, phenyloxy,
20 methoxy and ethoxy; and

wherein R² is one or more substituents independently
selected from H, chloro, fluoro, bromo, amino,
hydroxy, methyl, ethyl, propyl, trifluoromethyl,
methoxy, ethoxy, trifluoromethoxy, carboxymethyl,
25 unsubstituted or substituted phenyl and unsubstituted
or substituted heteroaryl selected
from thienyl, furanyl, pyridyl, imidazolyl, and
pyrazolyl;

and pharmaceutically acceptable salts thereof.

27. A compound of Claim 1 having the formula



wherein A^5 is selected from S, O and NR^6 ;

wherein R^a and R^b are independently selected from H, halo,

5 C_{1-4} -alkyl and $-N(R^6)_2$;

wherein n is 1-2;

wherein R is selected from

a) unsubstituted or substituted 5- or 6-membered
nitrogen-containing heteroaryl, and

10 b) unsubstituted or substituted 9- or 10-membered
fused nitrogen-containing heteroaryl,

where R is substituted with one or more substituents
selected from halo, amino, hydroxy, C_{1-6} -alkyl, C_{1-6} -
haloalkyl and C_{1-6} -alkoxy;

15 wherein R^1 is selected from unsubstituted or substituted
aryl,

5-6 membered heteroaryl and

9-10 membered fused heteroaryl,

wherein substituted R^1 is substituted with one or more

20 substituents selected from halo, C_{1-6} -alkyl, optionally
substituted C_{3-6} -cycloalkyl, optionally substituted
phenyl, C_{1-6} -haloalkoxy, optionally substituted
phenyloxy, benzyl, optionally substituted 5-6 membered
heterocyclyl- C_1 - C_2 -alkylenyl, optionally substituted
25 heteroaryl, optionally substituted heteroaryloxy, C_{1-6} -
haloalkyl, and C_{1-6} -alkoxy;

wherein R^2 is one or more substituents independently
selected from

H,

30 halo,

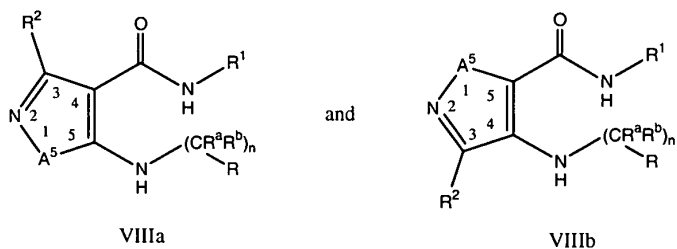
Approved for Release by NSA on 09-08-2013 pursuant to E.O. 13526

- C₁₋₆-alkyl,
C₁₋₆-haloalkyl,
C₁₋₆-alkoxy,
C₁₋₆-haloalkoxy,
5 C₁₋₆-carboxyalkyl,
unsubstituted or substituted aryl and
unsubstituted or substituted 5-6 membered
heteroaryl; and
wherein R⁶ is H or C₁₋₆-alkyl;
10 and pharmaceutically acceptable isomers and salts thereof.
28. Compound of Claim 27 wherein R^a and R^b are H;
wherein n is 1-2;
wherein R is selected from 4-pyridyl, pyrimidinyl,
15 pyridazinyl, indolyl, isoindolyl, indazolyl, quinolyl,
isoquinolyl, naphthyridinyl and quinoxalinyl, where R
is unsubstituted or substituted with one or more
substituents selected
from chloro, fluoro, amino, hydroxy, methyl, ethyl,
20 propyl, trifluoromethyl, methoxy and ethoxy;
wherein R¹ is selected from phenyl, tetrahydronaphthyl,
naphthyl, isoquinolyl, quinolyl, pyridyl, pyrimidinyl,
pyridazinyl, indolyl, isoindolyl, naphthyridinyl,
quinoxalinyl, tetrahydroquinolinyl, indazolyl,
25 benzothienyl, benzofuryl, benzimidazolyl,
benzoxazolyl, or benzthiazolyl, where R¹ is
unsubstituted or substituted with one or more
substituents selected
from chloro, fluoro, amino, hydroxy, cyclohexyl,
30 phenylmethyl, morpholinylmethyl,
methylpiperidinylmethyl, methylpiperazinylmethyl,
ethyl, propyl, trifluoromethyl, phenyloxy,
methoxy and ethoxy; and

wherein R^2 is one or more substituents independently
 selected from H, chloro, fluoro, bromo, amino,
 hydroxy, methyl, ethyl, propyl, trifluoromethyl,
 methoxy, ethoxy, trifluoromethoxy, carboxymethyl,
 5 unsubstituted or substituted phenyl and unsubstituted
 or substituted heteroaryl selected
 from thienyl, furanyl, pyridyl, imidazolyl, and
 pyrazolyl;
 and pharmaceutically acceptable salts thereof.

10

29. Compound of Claim 1 of the formulas



- 15 wherein A^5 is selected from S, O and NR^6 ;
 wherein R^a and R^b are independently selected from H, halo,
 C_{1-4} -alkyl and $-N(R^6)_2$;
 wherein n is 1-2;
 wherein R is selected from
- 20 a) unsubstituted or substituted 5- or 6-membered
 nitrogen-containing heteroaryl, and
 b) unsubstituted or substituted 9- or 10-membered
 fused nitrogen-containing heteroaryl,
 where R is substituted with one or more substituents
- 25 selected from halo, amino, hydroxy, C_{1-6} -alkyl, C_{1-6} -haloalkyl and C_{1-6} -alkoxy;
 wherein R^1 is selected from unsubstituted or substituted
 aryl,
 5-6 membered heteroaryl and
- 30 9-10 membered fused heteroaryl,

wherein substituted R¹ is substituted with one or more
substituents selected from halo, C₁₋₆-alkyl, optionally
substituted C₃₋₆-cycloalkyl, optionally substituted
phenyl, C₁₋₆-haloalkoxy, optionally substituted
5 phenyloxy, benzyl, optionally substituted 5-6 membered
heterocyclyl-C₁-C₂-alkylenyl, optionally substituted
heteroaryl, optionally substituted heteroaryloxy, C₁₋₆-
haloalkyl, and C₁₋₆-alkoxy;

wherein R² is one or more substituents independently
10 selected from

H,
halo,
C₁₋₆-alkyl,
C₁₋₆-haloalkyl,
15 C₁₋₆-alkoxy,
C₁₋₆-haloalkoxy,
C₁₋₆-carboxyalkyl,
unsubstituted or substituted aryl and
unsubstituted or substituted 5-6 membered
20 heteroaryl; and

wherein R⁶ is H or C₁₋₆-alkyl;

and pharmaceutically acceptable isomers and salts thereof.

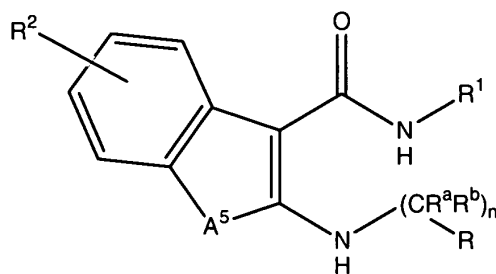
30. Compound of Claim 29 wherein R^a and R^b are H;

25 wherein n is 1-2;

wherein R is selected from 4-pyridyl, pyrimidinyl,
pyridazinyl, indolyl, isoindolyl, indazolyl, quinolyl,
isoquinolyl, naphthyridinyl and quinoxalyl, where R
is unsubstituted or substituted with one or more
30 substituents selected
from chloro, fluoro, amino, hydroxy, methyl, ethyl,
propyl, trifluoromethyl, methoxy and ethoxy;
wherein R¹ is selected from phenyl, tetrahydronaphthyl,
naphthyl, isoquinolyl, quinolyl, pyridyl, pyrimidinyl,

- pyridazinyl, indolyl, isoindolyl, naphthyridinyl,
quinoxaliny, tetrahydroquinoliny, indazolyl,
benzothienyl, benzofuryl, benzimidazolyl,
benzoxazolyl, or benzthiazolyl, where R¹ is
5 unsubstituted or substituted with one or more
substituents selected
from chloro, fluoro, amino, hydroxy, cyclohexyl,
phenylmethyl, morpholinylmethyl,
methylpiperidinylmethyl, methylpiperazinylmethyl,
10 ethyl, propyl, trifluoromethyl, phenoxy,
methoxy and ethoxy; and
wherein R² is one or more substituents independently
selected from H, chloro, fluoro, bromo, amino,
hydroxy, methyl, ethyl, propyl, trifluoromethyl,
15 methoxy, ethoxy, trifluoromethoxy, carboxymethyl,
unsubstituted or substituted phenyl and unsubstituted
or substituted heteroaryl selected
from thienyl, furanyl, pyridyl, imidazolyl, and
pyrazolyl;
20 and pharmaceutically acceptable salts thereof.

31. Compound of Claim 1 of the formula



- 25 wherein A⁵ is selected from S, O and NR⁶;
wherein R^a and R^b are independently selected from H, halo,
C₁₋₄-alkyl and -N(R⁶)₂;
wherein n is 1-2;

wherein R is selected from

- a) unsubstituted or substituted 5- or 6-membered
nitrogen-containing heteroaryl, and
- b) unsubstituted or substituted 9- or 10-membered
fused nitrogen-containing heteroaryl,

where R is substituted with one or more substituents
selected from halo, amino, hydroxy, C₁₋₆-alkyl, C₁₋₆-haloalkyl and C₁₋₆-alkoxy;

wherein R¹ is selected from unsubstituted or substituted
aryl,

5-6 membered heteroaryl and
9-10 membered fused heteroaryl,

wherein substituted R¹ is substituted with one or more
substituents selected from halo, C₁₋₆-alkyl, optionally
substituted C₃₋₆-cycloalkyl, optionally substituted
phenyl, C₁₋₆-haloalkoxy, optionally substituted
phenyloxy, benzyl, optionally substituted 5-6 membered
heterocyclyl-C₁₋₂-alkylenyl, optionally substituted
heteroaryl, optionally substituted heteroaryloxy, C₁₋₆-
haloalkyl, and C₁₋₆-alkoxy;

wherein R² is one or more substituents independently
selected from

H,
halo,
C₁₋₆-alkyl,
C₁₋₆-haloalkyl,
C₁₋₆-alkoxy,
C₁₋₆-haloalkoxy,
C₁₋₆-carboxyalkyl,

unsubstituted or substituted aryl and
unsubstituted or substituted 5-6 membered
heteroaryl; and

wherein R⁶ is H or C₁₋₆-alkyl;

and pharmaceutically acceptable isomers and salts thereof.

32. Compound of Claim 31 wherein R^a and R^b are H;
wherein n is 1-2;

wherein R is selected from 4-pyridyl, pyrimidinyl,

5 pyridazinyl, indolyl, isoindolyl, indazolyl, quinolyl,
isoquinolyl, naphthyridinyl and quinozaliny, where R
is unsubstituted or substituted with one or more
substituents selected

10 from chloro, fluoro, amino, hydroxy, methyl, ethyl,
propyl, trifluoromethyl, methoxy and ethoxy;

wherein R¹ is selected from phenyl, tetrahydronaphthyl,

15 naphthyl, isoquinolyl, quinolyl, pyridyl, pyrimidinyl,
pyridazinyl, indolyl, isoindolyl, naphthyridinyl,
quinozaliny, tetrahydroquinolinyl, indazolyl,
benzothienyl, benzofuryl, benzimidazolyl,
benzoxazolyl, or benzthiazolyl, where R¹ is
unsubstituted or substituted with one or more
substituents selected

20 from chloro, fluoro, amino, hydroxy, cyclohexyl,
phenylmethyl, morpholinylmethyl,
methylnpiperdinylmethyl, methylnpiperazinylmethyl,
ethyl, propyl, trifluoromethyl, phenyloxy,
methoxy and ethoxy; and

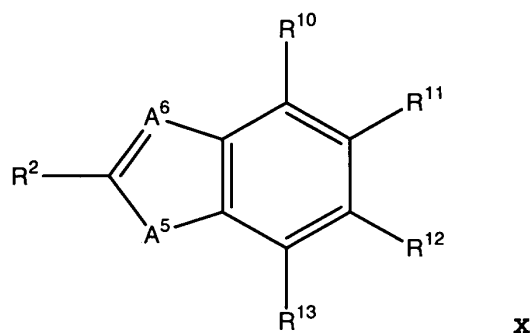
wherein R² is one or more substituents independently

25 selected from H, chloro, fluoro, bromo, amino,
hydroxy, methyl, ethyl, propyl, trifluoromethyl,
methoxy, ethoxy, trifluoromethoxy, carboxymethyl,
unsubstituted or substituted phenyl and unsubstituted
or substituted heteroaryl selected

30 from thienyl, furanyl, pyridyl, imidazolyl, and
pyrazolyl;

and pharmaceutically acceptable salts thereof.

33. Compound of Claim 1 of the formula



wherein A⁵ is selected from S, O and NR⁶;

5 wherein A⁶ is selected from CR² and N;

wherein R is selected from

a) unsubstituted or substituted 5- or 6-membered
nitrogen-containing heteroaryl, and

10 b) unsubstituted or substituted 9- or 10-membered
fused nitrogen-containing heteroaryl,

where R is substituted with one or more substituents
selected from halo, amino, hydroxy, C₁₋₆-alkyl, C₁₋₆-
haloalkyl and C₁₋₆-alkoxy;

15 wherein R¹ is selected from unsubstituted or substituted
aryl,

5-6 membered heteroaryl and

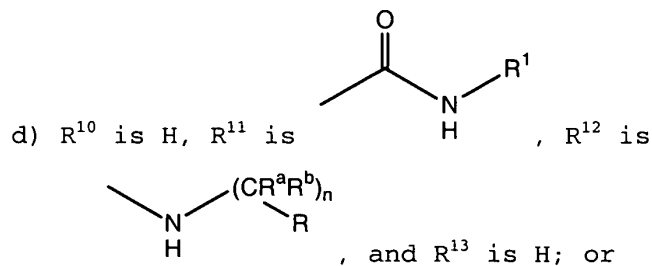
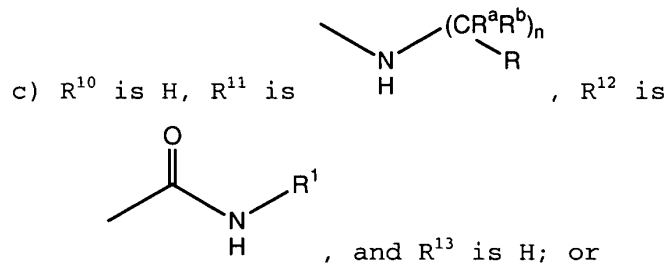
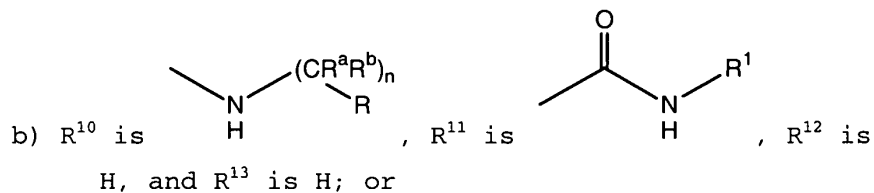
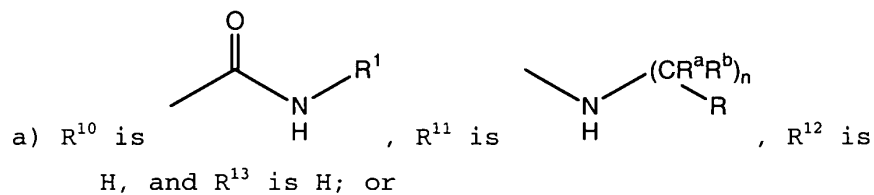
9-10 membered fused heteroaryl,

20 wherein substituted R¹ is substituted with one or more
substituents selected from halo, C₁₋₆-alkyl, optionally
substituted C₃₋₆-cycloalkyl, optionally substituted
phenyl, C₁₋₆-haloalkoxy, optionally substituted
phenyloxy, benzyl, optionally substituted 5-6 membered
heterocyclyl-C₁-C₂-alkylenyl, optionally substituted
heteroaryl, optionally substituted heteroaryloxy, C₁₋₆-
25 haloalkyl, and C₁₋₆-alkoxy;

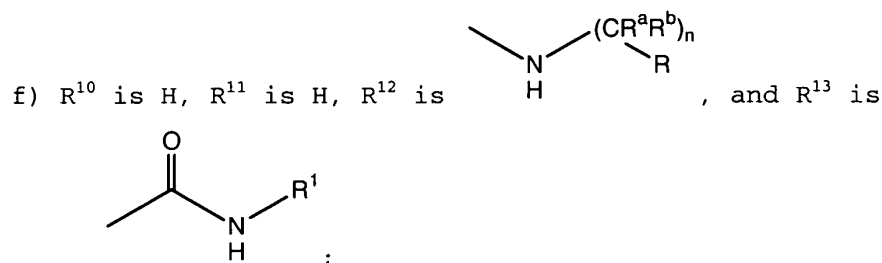
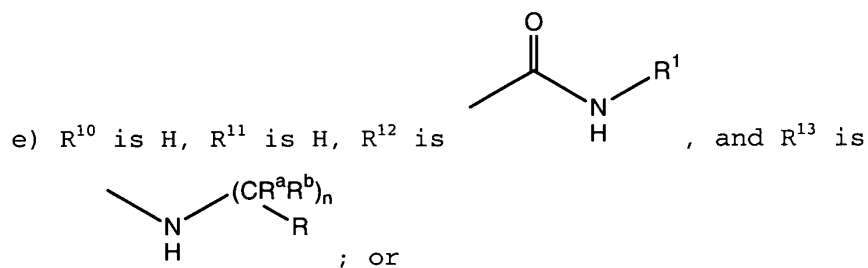
wherein R² is one or more substituents independently
selected from

H,

- halo,
 C₁₋₆-alkyl,
 C₁₋₆-haloalkyl,
 C₁₋₆-alkoxy,
 C₁₋₆-haloalkoxy,
 C₁₋₆-carboxyalkyl,
 unsubstituted or substituted aryl and
 unsubstituted or substituted 5-6 membered
 heteroaryl; and
 wherein R⁶ is H or C₁₋₆-alkyl;
 wherein



1001694-0100
 20010100-0100
 20010100-0100



5

wherein R^a and R^b are independently selected from H, halo, C_{1-4} -alkyl and $-N(R^6)_2$; and

wherein n is 1-2;

and pharmaceutically acceptable isomers and salts thereof.

10

34. Compound of Claim 33 wherein R^a and R^b are H; wherein n is 1-2;

wherein R is selected from 4-pyridyl, pyrimidinyl, pyridazinyl, indolyl, isoindolyl, indazolyl, quinolyl, isoquinolyl, naphthyridinyl and quinoxalinyl, where R is unsubstituted or substituted with one or more substituents selected from chloro, fluoro, amino, hydroxy, methyl, ethyl, propyl, trifluoromethyl, methoxy and ethoxy;

15

wherein R^1 is selected from phenyl, tetrahydronaphthyl, naphthyl, isoquinolyl, quinolyl, pyridyl, pyrimidinyl, pyridazinyl, indolyl, isoindolyl, naphthyridinyl, quinoxalinyl, tetrahydroquinolyl, indazolyl, benzothienyl, benzofuryl, benzimidazolyl, benzoxazolyl, or benzthiazolyl, where R^1 is

25

"SECRET" TEST COPY

unsubstituted or substituted with one or more
substituents selected

from chloro, fluoro, amino, hydroxy, cyclohexyl,
phenylmethyl, morpholinylmethyl,

5 methylpiperidinylmethyl, methylpiperazinylmethyl,
ethyl, propyl, trifluoromethyl, phenyloxy,
methoxy and ethoxy; and

wherein R^2 is one or more substituents independently

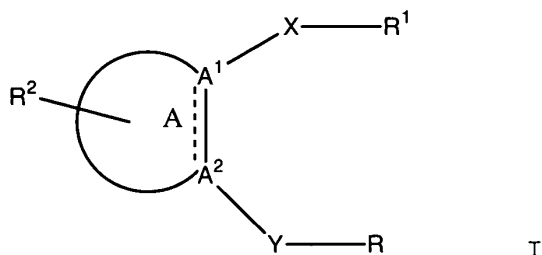
selected from H, chloro, fluoro, bromo, amino,
10 hydroxy, methyl, ethyl, propyl, trifluoromethyl,
methoxy, ethoxy, trifluoromethoxy, carboxymethyl,
unsubstituted or substituted phenyl and unsubstituted
or substituted heteroaryl selected
from thienyl, furanyl, pyridyl, imidazolyl, and
15 pyrazolyl;

and pharmaceutically acceptable salts thereof.

35. A pharmaceutical composition comprising a
pharmaceutically-acceptable carrier and a compound as in any
20 of Claims 1-34.

36. A method of treating cancer in a subject, said
method comprising administering an effective amount of a
compound of formula I

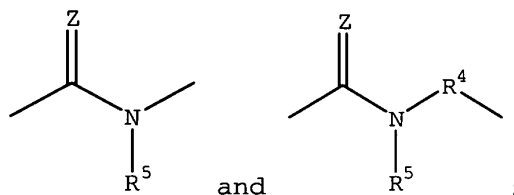
25



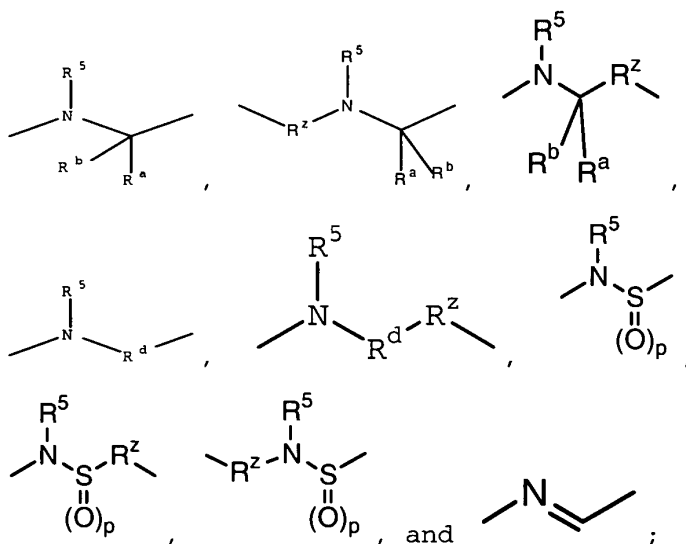
wherein each of A^1 and A^2 is independently C or N;
wherein ring A is selected from

- a) 5- or 6-membered partially saturated heterocyclyl,
 b) 5- or 6-membered heteroaryl,
 c) 9- or 10-membered fused partially saturated heterocyclyl,
 5 d) 9-, 10- or 11-membered fused heteroaryl;
 e) naphthyl, and
 f) 4-, 5- or 6- membered cycloalkenyl;

wherein X is selected from



- 10 wherein Z is oxygen or sulfur;
 wherein Y is selected from



- 15 wherein p is 0 to 2,
 wherein R^a and R^b are independently selected from H, halo,
 cyano, -NHR⁶ and C₁₋₄-alkyl substituted with R², or wherein
 R^a and R^b together form C₃-C₆ cycloalkyl;
 wherein R^z is selected from C₁-C₄ alkylenyl, where one of the
 20 CH₂ groups may be substituted with an oxygen atom or an -
 NH-;

wherein R^d is cycloalkyl;

wherein R is selected from

a) substituted or unsubstituted 5-6 membered heterocyclyl, and

5 b) substituted or unsubstituted fused 9-, 10- or 11-membered heterocyclyl;

wherein substituted R is substituted with one or more substituents independently selected from halo, -OR³, -SR³, -SO₂R³, -CO₂R³, -CONR³R³, -COR³, -NR³R³, -SO₂NR³R³,
10 -NR³C(O)OR³, -NR³C(O)R³, cycloalkyl, optionally substituted 5-6 membered heterocyclyl, optionally substituted phenyl, lower alkyl substituted with R², cyano, nitro, lower alkenyl and lower alkynyl;

wherein R¹ is selected from

15 a) substituted or unsubstituted 6-10 membered aryl,

b) substituted or unsubstituted 5-6 membered heterocyclyl,

c) substituted or unsubstituted 9-11 membered fused heterocyclyl,

20 d) cycloalkyl, and

e) cycloalkenyl,

wherein substituted R¹ is substituted with one or more substituents independently selected from halo, -OR³, -SR³, -CO₂R³, -CONR³R³, -COR³, -NR³R³, -NH(C₁-C₄
25 alkylenylR¹⁴), -SO₂R³, -SO₂NR³R³, -NR³C(O)OR³, -NR³C(O)R³, optionally substituted cycloalkyl, optionally substituted 5-6 membered heterocyclyl, optionally substituted phenyl, lower alkyl substituted with R², cyano, nitro, lower alkenyl and
30 lower alkynyl;

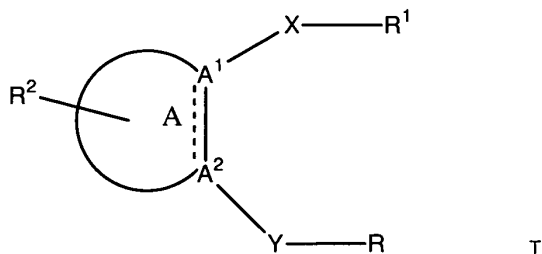
wherein R² is one or more substituents independently selected from H, halo, -OR³, oxo, -SR³, -CO₂R³, -COR³, -CONR³R³, -NR³R³, -SO₂NR³R³, -NR³C(O)OR³, -NR³C(O)R³, cycloalkyl, optionally substituted phenylalkylenyl, optionally

404569 0400
EOT FOR 100

substituted 5-6 membered heterocyclyl, optionally substituted heteroarylalkylenyl, optionally substituted phenyl, lower alkyl, cyano, lower hydroxyalkyl, lower carboxyalkyl, nitro, lower alkenyl, lower alkynyl, lower aminoalkyl, lower alkylaminoalkyl and lower haloalkyl; wherein R³ is selected from H, lower alkyl, phenyl, 5-6 membered heterocyclyl, C₃-C₆ cycloalkyl, and lower haloalkyl; wherein R⁴ is independently selected from C₂-C₄ alkylenyl, C₂-C₄ alkenylenyl and C₂-C₄ alkynylenyl, where one of the CH₂ groups may be substituted with an oxygen atom or an -NH-; wherein R⁵ is selected from H, lower alkyl, phenyl and lower aralkyl; and wherein R⁶ is selected from H or C₁₋₆-alkyl; wherein R¹⁴ is selected from H, phenyl, 5-6 membered heterocyclyl and C₃-C₆ cycloalkyl; and pharmaceutically acceptable salts thereof; provided A is not naphthyl when X is -C(O)NH- and when R¹ is phenyl when Y is -NCH₂- and when R is 4-pyridyl; and further provided R is not unsubstituted 2-thienyl, 2-pyridyl or 3-pyridyl when Y is -NHCH₂-.

37. The method of Claim 36 comprising a combination with a compound selected from antibiotic-type agents, alkylating agents, antimetabolite agents, hormonal agents, immunological agents, interferon-type agents and miscellaneous agents.

38. A method of treating angiogenesis in a subject, said method comprising administering an effective amount of a compound as in any of Formula I

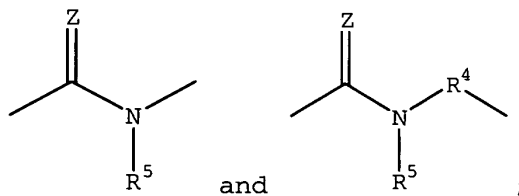


wherein each of A^1 and A^2 is independently C or N;

wherein ring A is selected from

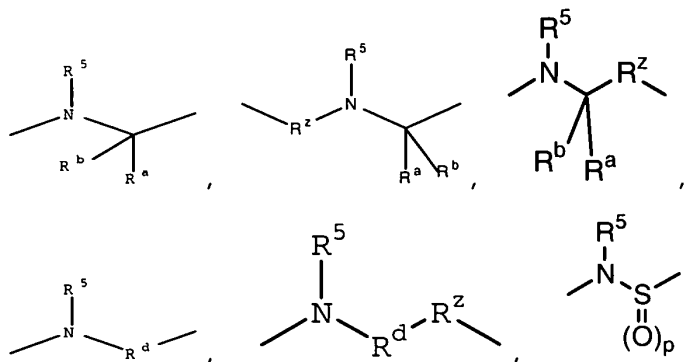
- 5 a) 5- or 6-membered partially saturated heterocyclyl,
 b) 5- or 6-membered heteroaryl,
 c) 9- or 10-membered fused partially saturated
 heterocyclyl,
 d) 9-, 10- or 11-membered fused heteroaryl;
 10 e) naphthyl, and
 f) 4-, 5- or 6- membered cycloalkenyl;

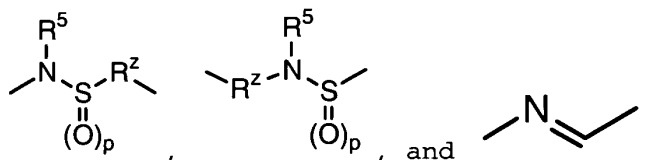
wherein X is selected from



wherein Z is oxygen or sulfur;

- 15 wherein Y is selected from





wherein p is 0 to 2,

wherein R^a and R^b are independently selected from H, halo, cyano, -NHR⁶ and C₁₋₄-alkyl substituted with R², or wherein

5 R^a and R^b together form C_3 - C_6 cycloalkyl;

wherein R² is selected from C₁-C₄ alkylenyl, where one of the CH₂ groups may be substituted with an oxygen atom or an -NH-;

wherein R^d is cycloalkyl;

10 wherein R is selected from

a) substituted or unsubstituted 5-6 membered heterocyclyl, and

b) substituted or unsubstituted fused 9-, 10- or 11-membered heterocyclyl;

15 wherein substituted R is substituted with one or more
substituents independently selected from halo, -OR³,
-SR³, -SO₂R³, -CO₂R³, -CONR³R³, -COR³, -NR³R³, -SO₂NR³R³,
-NR³C(O)OR³, -NR³C(O)R³, cycloalkyl, optionally
substituted 5-6 membered heterocyclyl, optionally
20 substituted phenyl, lower alkyl substituted with R²,
cyano, nitro, lower alkenyl and lower alkynyl;

wherein R^1 is selected from

a) substituted or unsubstituted 6-10 membered aryl,

b) substituted or unsubstituted 5-6 membered
25 heterocyclyl,

c) substituted or unsubstituted 9-11 membered fused heterocyclyl,

d) cycloalkyl, and

e) cycloalkenyl,

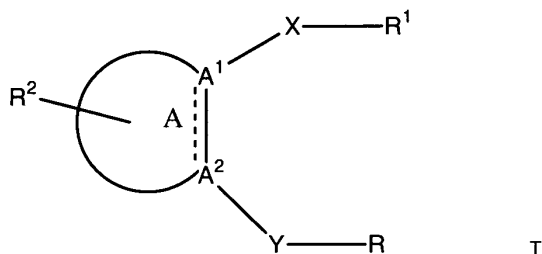
30 wherein substituted R¹ is substituted with one or more
substituents independently selected from halo, -OR³,

- SR³, -CO₂R³, -CONR³R³, -COR³, -NR³R³, -NH(C₁-C₄ alkylenylR¹⁴), -SO₂R³, -SO₂NR³R³, -NR³C(O)OR³, -NR³C(O)R³, optionally substituted cycloalkyl, optionally substituted 5-6 membered heterocyclyl, optionally substituted phenyl, lower alkyl substituted with R², cyano, nitro, lower alkenyl and lower alkynyl;
- wherein R² is one or more substituents independently selected from H, halo, -OR³, oxo, -SR³, -CO₂R³, -COR³, -CONR³R³, -NR³R³, -SO₂NR³R³, -NR³C(O)OR³, -NR³C(O)R³, cycloalkyl, optionally substituted phenylalkylenyl, optionally substituted 5-6 membered heterocyclyl, optionally substituted heteroarylalkylenyl, optionally substituted phenyl, lower alkyl, cyano, lower hydroxyalkyl, lower carboxyalkyl, nitro, lower alkenyl, lower alkynyl, lower aminoalkyl, lower alkylaminoalkyl and lower haloalkyl;
- wherein R³ is selected from H, lower alkyl, phenyl, 5-6 membered heterocyclyl, C₃-C₆ cycloalkyl, and lower haloalkyl;
- wherein R⁴ is independently selected from C₂-C₄ alkylenyl, C₂-C₄ alkenylenyl and C₂-C₄ alkynylenyl, where one of the CH₂ groups may be substituted with an oxygen atom or an -NH-;
- wherein R⁵ is selected from H, lower alkyl, phenyl and lower aralkyl; and
- wherein R⁶ is selected from H or C₁₋₆-alkyl;
- wherein R¹⁴ is selected from H, phenyl, 5-6 membered heterocyclyl and C₃-C₆ cycloalkyl;
- and pharmaceutically acceptable salts thereof;
- provided A is not naphthyl when X is -C(O)NH- and when R¹ is phenyl when Y is -NCH₂- and when R is 4-pyridyl; and further provided R is not unsubstituted 2-thienyl, 2-pyridyl or 3-pyridyl when Y is -NHCH₂-.

20040404 10:45:04

39. A compound as in any of Claims 1-34 for use in a method of therapeutic treatment for the human or animal body.

- 5 40. A method of treating KDR-related disorders in a mammal, said method comprising administering an effective amount of a compound of Formula I

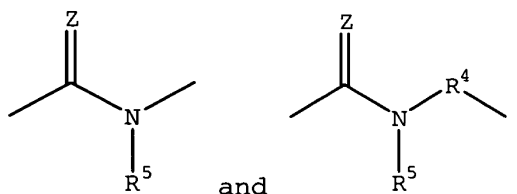


10

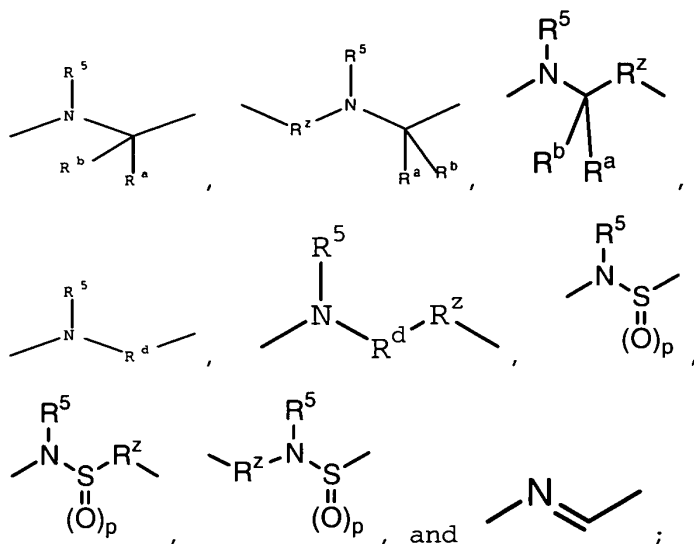
wherein each of A¹ and A² is independently C or N;
wherein ring A is selected from

- a) 5- or 6-membered partially saturated heterocyclyl,
b) 5- or 6-membered heteroaryl,
15 c) 9- or 10-membered fused partially saturated heterocyclyl,
d) 9-, 10- or 11-membered fused heteroaryl;
e) naphthyl, and
f) 4-, 5- or 6- membered cycloalkenyl;

20 wherein X is selected from



wherein Z is oxygen or sulfur;
wherein Y is selected from



wherein p is 0 to 2,

- 5 wherein R^a and R^b are independently selected from H, halo, cyano, $-NHR^6$ and C_{1-4} -alkyl substituted with R^2 , or wherein R^a and R^b together form C_3 - C_6 cycloalkyl;

wherein R^z is selected from C_1 - C_4 alkylene, where one of the CH_2 groups may be substituted with an oxygen atom or an -

10 NH-;

wherein R^d is cycloalkyl;

wherein R is selected from

- a) substituted or unsubstituted 5-6 membered heterocyclyl, and
- 15 b) substituted or unsubstituted fused 9-, 10- or 11-membered heterocyclyl;
- wherein substituted R is substituted with one or more substituents independently selected from halo, $-OR^3$, $-SR^3$, $-SO_2R^3$, $-CO_2R^3$, $-CONR^3R^3$, $-COR^3$, $-NR^3R^3$, $-SO_2NR^3R^3$, $-NR^3C(O)OR^3$, $-NR^3C(O)R^3$, cycloalkyl, optionally
- 20 substituted 5-6 membered heterocyclyl, optionally substituted phenyl, lower alkyl substituted with R^2 , cyano, nitro, lower alkenyl and lower alkynyl;

wherein R^1 is selected from

- 25 a) substituted or unsubstituted 6-10 membered aryl,

- b) substituted or unsubstituted 5-6 membered heterocyclyl,
c) substituted or unsubstituted 9-11 membered fused heterocyclyl,
5 d) cycloalkyl, and
e) cycloalkenyl,

wherein substituted R^1 is substituted with one or more substituents independently selected from halo, $-OR^3$, $-SR^3$, $-CO_2R^3$, $-CONR^3R^3$, $-COR^3$, $-NR^3R^3$, $-NH(C_1-C_4$
10 alkylenyl $R^{14})$, $-SO_2R^3$, $-SO_2NR^3R^3$, $-NR^3C(O)OR^3$, $-NR^3C(O)R^3$, optionally substituted cycloalkyl, optionally substituted 5-6 membered heterocyclyl, optionally substituted phenyl, lower alkyl substituted with R^2 , cyano, nitro, lower alkenyl and
15 lower alkynyl;

wherein R^2 is one or more substituents independently selected from H, halo, $-OR^3$, oxo, $-SR^3$, $-CO_2R^3$, $-COR^3$, $-CONR^3R^3$, $-NR^3R^3$, $-SO_2NR^3R^3$, $-NR^3C(O)OR^3$, $-NR^3C(O)R^3$, cycloalkyl, optionally substituted phenylalkylenyl, optionally
20 substituted 5-6 membered heterocyclyl, optionally substituted heteroarylalkylenyl, optionally substituted phenyl, lower alkyl, cyano, lower hydroxyalkyl, lower carboxyalkyl, nitro, lower alkenyl, lower alkynyl, lower aminoalkyl, lower alkylaminoalkyl and lower haloalkyl;

25 wherein R^3 is selected from H, lower alkyl, phenyl, 5-6 membered heterocyclyl, C_3-C_6 cycloalkyl, and lower haloalkyl;

wherein R^4 is independently selected from C_2-C_4 alkylenyl, C_2-C_4 alkenylenyl and C_2-C_4 alkynylenyl, where one of the
30 CH_2 groups may be substituted with an oxygen atom or an $-NH-$;

wherein R^5 is selected from H, lower alkyl, phenyl and lower aralkyl; and

wherein R^6 is selected from H or C_{1-6} -alkyl;

2004554 0100
E00110 153100

wherein R^{14} is selected from H, phenyl, 5-6 membered

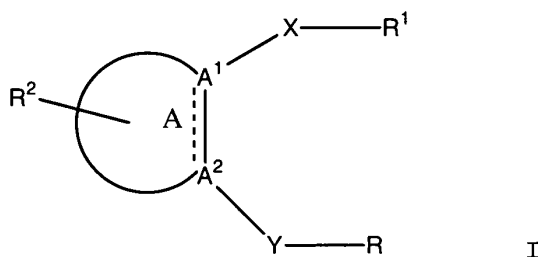
heterocyclyl and C_3-C_6 cycloalkyl;

and pharmaceutically acceptable salts thereof;

provided A is not naphthyl when X is $-C(O)NH-$ and when R^1 is

- 5 phenyl when Y is $-NCH_2-$ and when R is 4-pyridyl; and further
provided R is not unsubstituted 2-thienyl, 2-pyridyl or 3-
pyridyl when Y is $-NHCH_2-$.

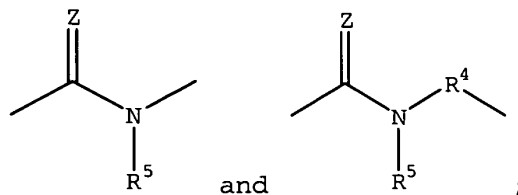
41. A method of treating proliferative disorders in a
10 mammal, said method comprising administering an effective
amount of a compound of Formula I



- 15 wherein each of A^1 and A^2 is independently C or N;
wherein ring A is selected from

- a) 5- or 6-membered partially saturated heterocyclyl,
b) 5- or 6-membered heteroaryl,
c) 9- or 10-membered fused partially saturated
20 heterocyclyl,
d) 9-, 10- or 11-membered fused heteroaryl;
e) naphthyl, and
f) 4-, 5- or 6- membered cycloalkenyl;

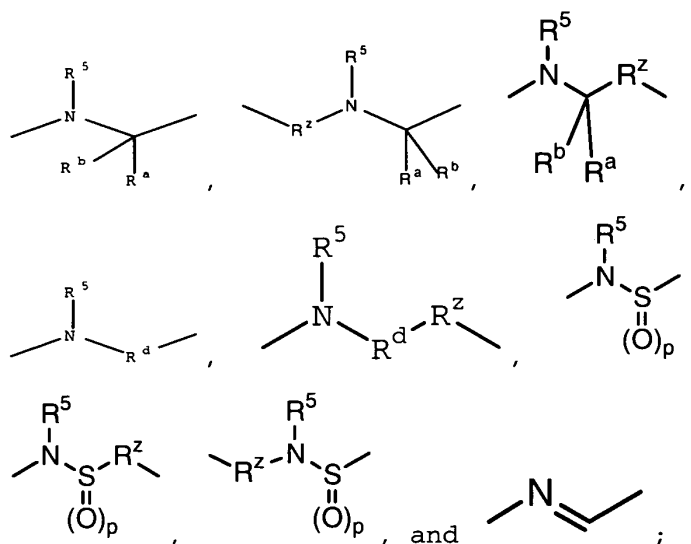
wherein X is selected from



25

wherein Z is oxygen or sulfur;

wherein Y is selected from



5 wherein p is 0 to 2,

wherein R^a and R^b are independently selected from H, halo, cyano, $-\text{NHR}^6$ and C_{1-4} -alkyl substituted with R^2 , or wherein R^a and R^b together form C_3 - C_6 cycloalkyl;

10 wherein R^z is selected from C_1 - C_4 alkylene, where one of the CH_2 groups may be substituted with an oxygen atom or an $-\text{NH}-$;

wherein R^d is cycloalkyl;

wherein R is selected from

15 a) substituted or unsubstituted 5-6 membered heterocyclyl, and

b) substituted or unsubstituted fused 9-, 10- or 11-membered heterocyclyl;

20 wherein substituted R is substituted with one or more substituents independently selected from halo, $-\text{OR}^3$, $-\text{SR}^3$, $-\text{SO}_2\text{R}^3$, $-\text{CO}_2\text{R}^3$, $-\text{CONR}^3\text{R}^3$, $-\text{COR}^3$, $-\text{NR}^3\text{R}^3$, $-\text{SO}_2\text{NR}^3\text{R}^3$, $-\text{NR}^3\text{C}(\text{O})\text{OR}^3$, $-\text{NR}^3\text{C}(\text{O})\text{R}^3$, cycloalkyl, optionally substituted 5-6 membered heterocyclyl, optionally substituted phenyl, lower alkyl substituted with R^2 , cyano, nitro, lower alkenyl and lower alkynyl;

25 wherein R^1 is selected from

- a) substituted or unsubstituted 6-10 membered aryl,
b) substituted or unsubstituted 5-6 membered heterocyclyl,
c) substituted or unsubstituted 9-11 membered fused
5 heterocyclyl,
d) cycloalkyl, and
e) cycloalkenyl,
wherein substituted R^1 is substituted with one or more substituents independently selected from halo, $-OR^3$,
10 $-SR^3$, $-CO_2R^3$, $-CONR^3R^3$, $-COR^3$, $-NR^3R^3$, $-NH(C_1-C_4$ alkylenyl $R^{14})$, $-SO_2R^3$, $-SO_2NR^3R^3$, $-NR^3C(O)OR^3$, $-NR^3C(O)R^3$, optionally substituted cycloalkyl, optionally substituted 5-6 membered heterocyclyl, optionally substituted phenyl, lower alkyl
15 substituted with R^2 , cyano, nitro, lower alkenyl and lower alkynyl;
wherein R^2 is one or more substituents independently selected from H, halo, $-OR^3$, oxo, $-SR^3$, $-CO_2R^3$, $-COR^3$, $-CONR^3R^3$, $-NR^3R^3$, $-SO_2NR^3R^3$, $-NR^3C(O)OR^3$, $-NR^3C(O)R^3$, cycloalkyl,
20 optionally substituted phenylalkylenyl, optionally substituted 5-6 membered heterocyclyl, optionally substituted heteroarylalkylenyl, optionally substituted phenyl, lower alkyl, cyano, lower hydroxyalkyl, lower carboxyalkyl, nitro, lower alkenyl, lower alkynyl, lower
25 aminoalkyl, lower alkylaminoalkyl and lower haloalkyl;
wherein R^3 is selected from H, lower alkyl, phenyl, 5-6 membered heterocyclyl, C_3-C_6 cycloalkyl, and lower haloalkyl;
wherein R^4 is independently selected from C_2-C_4 alkylenyl,
30 C_2-C_4 alkenylenyl and C_2-C_4 alkynylenyl, where one of the CH_2 groups may be substituted with an oxygen atom or an $-NH-$;
wherein R^5 is selected from H, lower alkyl, phenyl and lower aralkyl; and

"SECRET"

wherein R^6 is selected from H or C_{1-6} -alkyl;

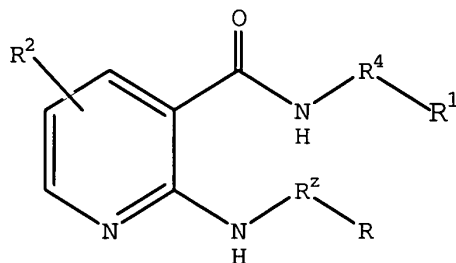
wherein R^{14} is selected from H, phenyl, 5-6 membered heterocyclyl and C_3 - C_6 cycloalkyl;

and pharmaceutically acceptable salts thereof;

- 5 provided A is not naphthyl when X is $-C(O)NH-$ and when R^1 is phenyl when Y is $-NCH_2-$ and when R is 4-pyridyl; and further provided R is not unsubstituted 2-thienyl, 2-pyridyl or 3-pyridyl when Y is $-NHCH_2-$.

- 10 42. Method of Claim 12 wherein the disorder is inflammation or an inflammation-related disorder.

43. A compound of Claim 1 having Formula II'



II'

wherein R is selected from

- a) unsubstituted or substituted 5- or 6-membered nitrogen-containing heteroaryl, and
- 20 b) unsubstituted or substituted 9- or 10-membered fused heteroaryl,
- where substituted R is substituted with one or more substituents selected from halo, amino, oxo, hydroxy, C_{1-6} -alkyl, C_{1-6} -haloalkyl, C_{1-6} -alkoxy, optionally substituted heterocyclyl- C_{1-6} -alkoxy, optionally substituted heterocyclyl- C_{1-6} -alkylamino, optionally substituted heterocyclyl- C_{1-6} -alkyl, C_{1-6} -alkylamino- C_{2-4} -alkynyl, C_{1-6} -alkylamino- C_{1-6} -alkoxy, C_{1-6} -alkylamino- C_{1-6} -alkoxy-
- 25

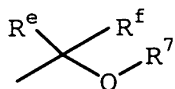
C₁₋₆-alkoxy, and optionally substituted
heterocyclyl-C₂₋₄-alkynyl;

wherein R¹ is selected from unsubstituted or substituted
aryl,

5 cycloalkyl,
 5-6 membered heteroaryl and
 9-10 membered bicyclic and 13-14 membered
 tricyclic heterocyclyl,

wherein substituted R¹ is substituted with one or more

10 substituents selected from halo, C₁₋₆-alkyl, optionally
 substituted C₃₋₆-cycloalkyl, optionally substituted
 phenyl, optionally substituted phenyl-C₁₋₄-alkylenyl,
 C₁₋₂-haloalkoxy, optionally substituted 4-6 membered
15 heterocyclyl-C₁₋₄-alkyl, optionally substituted 4-6
 membered heterocyclyl-C₂₋₄-alkenyl, optionally
 substituted 4-6 membered heterocyclyl, optionally
 substituted phenyloxy, optionally substituted 4-6
 membered heterocyclyloxy, optionally substituted 4-6
 membered heterocyclyl-C₁₋₄-alkoxy, optionally
20 substituted 4-6 membered heterocyclylsulfonyl,
 optionally substituted 4-6 membered heterocyclylamino,
 optionally substituted 4-6 membered
 heterocyclylcarbonyl, optionally substituted 5-6
 membered heterocyclyl-C₁₋₄-alkylcarbonyl, C₁₋₂-
25 haloalkyl, C₁₋₄-aminoalkyl, nitro, amino, hydroxy, oxo,
 cyano, -NHC(O)NH₂, alkylcarbonylamino, aminosulfonyl,
 C₁₋₂-alkylsulfonyl, halosulfonyl, C₁₋₄-alkylcarbonyl, C₁₋₃-
 alkylamino-C₁₋₃-alkyl, C₁₋₃-alkylamino-C₁₋₃-alkoxy, C₁₋₃-
 alkylamino-C₁₋₃-alkoxy-C₁₋₃-alkoxy, C₁₋₄-alkoxycarbonyl,
30 C₁₋₄-alkoxycarbonylamino-C₁₋₄-alkyl, C₁₋₄-hydroxyalkyl,

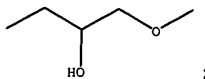


and C₁₋₄-alkoxy;

wherein R² is one or more substituents independently
selected from

H,
 halo,
 hydroxy,
 amino,
 5 C₁₋₆-alkyl,
 C₁₋₆-haloalkyl,
 C₁₋₆-alkoxy,
 C₁₋₂-alkylamino,
 aminosulfonyl,
 10 C₃₋₆-cycloalkyl,
 cyano,
 C₁₋₂-hydroxyalkyl,
 nitro,
 C₂₋₃-alkenyl,
 15 C₂₋₃-alkynyl,
 C₁₋₆-haloalkoxy,
 C₁₋₆-carboxyalkyl,
 5-6-membered heterocyclyl-C₁₋₆-alkylamino,
 unsubstituted or substituted phenyl and
 20 unsubstituted or substituted 5-6 membered
 heterocyclyl;

wherein R⁴ is selected from a direct bond, C₁₋₄-alkyl, and



wherein R² is selected from C₁₋₂-alkyl, C₂₋₆-branched alkyl,
 25 C₂₋₄-branched haloalkyl, amino-C₁₋₄-alkyl and C₁₋₂-
 alkylamino-C₁₋₂-alkyl;
 wherein R^e and R^f are independently selected from H and C₁₋₂-
 haloalkyl; and
 wherein R⁷ is selected from H, C₁₋₃-alkyl, optionally
 30 substituted phenyl, optionally substituted phenyl-C₁₋₃-
 alkyl, optionally substituted 4-6 membered
 heterocyclyl, optionally substituted 4-6 membered

heterocyclyl-C₁-C₃-alkyl, C₁₋₃-alkylamino-C₁₋₃-alkyl, C₁₋₃-alkoxy-C₁₋₂-alkyl and C₁₋₃-alkoxy-C₁₋₃-alkoxy-C₁₋₃-alkyl; provided R² is not H, or provided R¹ is not heteroaryl or aryl, or provided R is substituted with optionally substituted heterocyclyl-C₁₋₆-alkoxy, optionally substituted heterocyclyl-C₁₋₆-alkylamino, optionally substituted heterocyclyl-C₁₋₆-alkyl, C₁₋₆-alkylamino-C₂₋₄-alkynyl, C₁₋₆-alkylamino-C₁₋₆-alkoxy, C₁₋₆-alkylamino-C₁₋₆-alkoxy-C₁₋₆-alkoxy, or optionally substituted heterocyclyl-C₂₋₄-alkynyl, or provided R¹ is substituted with optionally substituted phenyloxy, optionally substituted 5-6 membered heterocyclyloxy, optionally substituted 5-6 membered heterocyclylsulfonyl, optionally substituted 5-6 membered heterocyclylamino, optionally substituted 5-6 membered heterocyclylcarbonyl, optionally substituted 5-6 membered heterocyclyl-C₁₋₄-alkylcarbonyl, C₁₋₃-alkylamino-C₁₋₃-alkoxy, or C₁₋₃-alkylamino-C₁₋₃-alkoxy-C₁₋₃-alkoxy; further provided R is not 3-pyridyl when R⁵ is CH₂; and pharmaceutically acceptable isomers and derivatives thereof.

44. Compound of Claim 43 wherein R is selected from 4-pyridyl, 3-pyridyl, 2-pyridyl, pyrimidinyl, triazolyl, pyridazinyl, indolyl, isoindolyl, indazolyl, quinolyl, isoquinolyl, benzotriazolyl, 2,3-dihydrobenzofuryl, 2-oxo-1,2-dihydroquinol-7-yl, naphthyridinyl and quinoxalinyl, where R is unsubstituted or substituted with one or more substituents selected from chloro, fluoro, amino, hydroxy, methyl, ethyl, propyl, trifluoromethyl, dimethylaminopropynyl, 1-methylpiperidinylmethoxy, dimethylaminoethoxyethoxy, methoxy and ethoxy; wherein R¹ is selected from phenyl, tetrahydronaphthyl, indanyl, indenyl,

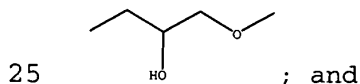
- naphthyl, cyclohexyl, isoxazolyl, pyrazolyl, thiazolyl, thiadiazolyl, thienyl, pyridyl, pyrimidinyl, pyridazinyl, 1,2-dihydroquinolyl, 1,2,3,4-tetrahydro-isoquinolyl, isoquinolyl, quinolyl, indolyl, isoindolyl, 2,3-dihydro-1H-indolyl, naphthyridinyl, quinoxalinyl, benzo[d]isothiazolyl, 2,3,4,4a,9,9a-hexahydro-1H-3-aza-fluorenyl, 5,6,7-trihydro-1,2,4-triazolo[3,4-a]isoquinolyl, tetrahydroquinolinyl, indazolyl, 2,1,3-benzothiadiazolyl, benzodioxanyl, benzothienyl, benzofuryl, dihydro-benzimidazolyl, benzimidazolyl, benzoxazolyl and benzthiazolyl, where R¹ is unsubstituted or substituted with one or more substituents selected from bromo, chloro, fluoro, iodo, nitro, amino, cyano, aminoethyl, Boc-aminoethyl, hydroxy, oxo, aminosulfonyl, 4-methylpiperazinylsulfonyl, cyclohexyl, phenyl, phenylmethyl, morpholinylmethyl, 1-methylpiperazin-4-ylmethyl, 1-methylpiperazin-4-ylpropyl, morpholinylpropyl, piperidin-1-ylmethyl, 1-methylpiperidin-4-ylmethyl, 2-methyl-2-(1-methylpiperidin-4-yl)ethyl, morpholinylethyl, 1-(4-morpholinyl)-2,2-dimethylpropyl, piperidin-4-ylethyl, 1-Boc-piperidin-4-ylethyl, piperidin-1-ylethyl, 1-Boc-piperidin-4-ylethyl, piperidin-4-ylmethyl, 1-Boc-piperidin-4-ylmethyl, piperidin-4-ylpropyl, 1-Boc-piperidin-4-ylpropyl, piperidin-1-ylpropyl, pyrrolidin-1-ylpropyl, pyrrolidin-2-ylpropyl, 1-Boc-pyrrolidin-2-ylpropyl, pyrrolidin-1-ylmethyl, pyrrolidin-2-ylmethyl, 1-Boc-pyrrolidin-2-ylmethyl, pyrrolidinylpropenyl, pyrrolidinylbutenyl, fluorosulfonyl, methylsulfonyl, methylcarbonyl, Boc, piperidin-1-ylmethylcarbonyl, 4-methylpiperazin-1-ylcarbonylethyl, methoxycarbonyl, aminomethylcarbonyl, dimethylaminomethylcarbonyl, 3-ethoxycarbonyl-2-methyl-fur-5-yl, 4-methylpiperazin-1-yl, 4-methyl-1-piperidyl, 1-Boc-4-piperidyl, piperidin-4-yl, 1-methylpiperidin-4-yl, 1-methyl-(1,2,3,6-tetrahydropyridyl), imidazolyl, morpholinyl, 4-trifluoromethyl-1-piperidinyl,

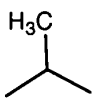
"SECRET"

- hydroxybutyl, methyl, ethyl, propyl, isopropyl, butyl, tert-butyl, sec-butyl, trifluoromethyl, pentafluoroethyl, nonafluorobutyl, dimethylaminopropyl, 1,1-di(trifluoromethyl)-1-hydroxymethyl, 1,1-
- 5 di(trifluoromethyl)-1-(piperidinylethoxy)methyl, 1,1-di(trifluoromethyl)-1-(methoxyethoxyethoxy)methyl, 1-hydroxyethyl, 2-hydroxyethyl, trifluoromethoxy, 1-aminoethyl, 2-aminoethyl, 1-(N-isopropylamino)ethyl, 2-(N-isopropylamino)ethyl, dimethylaminoethoxy, 4-chlorophenoxy,
- 10 phenoxy, azetidin-3-ylmethoxy, 1-Boc-azetidin-3-ylmethoxy, pyrrol-2-ylmethoxy, 1-Boc-pyrrol-2-ylmethoxy, pyrrol-1-ylmethoxy, 1-methyl-pyrrol-2-ylmethoxy, 1-isopropyl-pyrrol-2-ylmethoxy, 1-Boc-piperidin-4-ylmethoxy, piperidin-4-ylmethoxy, 1-methylpiperidin-4-ylmethoxy, isopropoxy, methoxy and
- 15 ethoxy; wherein R² is selected from H, chloro, fluoro, bromo, amino, hydroxy, methyl, ethyl, propyl, oxo, dimethylamino, aminosulfonyl, cyclopropyl, cyano, hydroxymethyl, nitro, propenyl, trifluoromethyl, methoxy, ethoxy, trifluoromethoxy, carboxymethyl,
- 20 morpholinylethylamino, propynyl, unsubstituted or substituted phenyl and unsubstituted or substituted heteroaryl selected from thienyl,

furanyl, pyridyl, imidazolyl, and pyrazolyl;

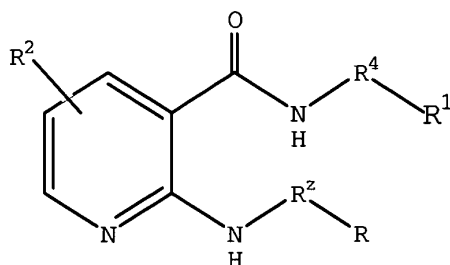
wherein R⁴ is selected from a direct bond, ethyl, butyl, and



wherein R² is selected from methylenyl, ethylenyl, , and aminoethylenyl;

and pharmaceutically acceptable derivatives thereof.

- 30 45. A compound of Claim 1 having Formula XI



wherein R is selected from

- a) unsubstituted or substituted 5- or 6-membered
nitrogen-containing heteroaryl, and
b) unsubstituted or substituted 9- or 10-membered
fused heteroaryl,

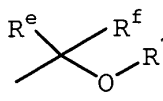
where substituted R is substituted with one or more
substituents selected from halo, amino, hydroxy,
C₁₋₆-alkyl, C₁₋₆-haloalkyl, C₁₋₆-alkoxy, optionally
substituted heterocyclyl-C₁₋₆-alkoxy, optionally
substituted heterocyclyl-C₁₋₆-alkylamino,
optionally substituted heterocyclyl-C₁₋₆-alkyl, C₁₋₆-
alkylamino-C₂₋₄-alkynyl, C₁₋₆-alkylamino-C₁₋₆-
alkoxy, C₁₋₆-alkylamino-C₁₋₆-alkoxy-C₁₋₆-alkoxy, and
optionally substituted heterocyclyl-C₂₋₄-alkynyl;

wherein R¹ is a ring selected from unsubstituted or
substituted

- 4-6 membered saturated or partially un-saturated
monocyclic heterocyclyl,
9-10 membered saturated or partially un-saturated
bicyclic heterocyclyl, and
13-14 membered saturated or partially un-
saturated tricyclic heterocyclyl,

wherein substituted R¹ is substituted with one or more
substituents selected from halo, C₁₋₆-alkyl, optionally
substituted C₃₋₆-cycloalkyl, optionally substituted
phenyl, optionally substituted phenyl-C₁₋₄-alkylenyl,
C₁₋₂-haloalkoxy, optionally substituted 4-6 membered

heterocyclyl-C₁-C₄-alkyl, optionally substituted 4-6
 membered heterocyclyl-C₂-C₄-alkenyl, optionally
 substituted 4-6 membered heterocyclyl, optionally
 substituted phenyloxy, optionally substituted 4-6
 5 membered heterocyclyloxy, optionally substituted 4-6
 membered heterocyclyl-C₁-C₄-alkoxy, optionally
 substituted 4-6 membered heterocyclylsulfonyl,
 optionally substituted 4-6 membered heterocyclylamino,
 optionally substituted 4-6 membered
 10 heterocyclylcarbonyl, optionally substituted 5-6
 membered heterocyclyl-C₁₋₄-alkylcarbonyl, C₁₋₂-
 haloalkyl, C₁₋₄-aminoalkyl, nitro, amino, hydroxy, oxo,
 cyano, aminosulfonyl, C₁₋₂-alkylsulfonyl, halosulfonyl,
 C₁₋₄-alkylcarbonyl, C₁₋₃-alkylamino-C₁₋₃-alkyl, C₁₋₃-
 15 alkylamino-C₁₋₃-alkoxy, C₁₋₃-alkylamino-C₁₋₃-alkoxy-C₁₋₃-
 alkoxy, C₁₋₄-alkoxycarbonyl, C₁₋₄-alkoxycarbonylamino-C₁₋

4-alkyl, C₁₋₄-hydroxyalkyl,  and C₁₋₄-alkoxy;

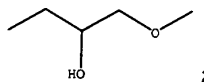
wherein R² is one or more substituents independently
 selected from

20 H,
 halo,
 hydroxy,
 amino,
 C₁₋₆-alkyl,
 25 C₁₋₆-haloalkyl,
 C₁₋₆-alkoxy,
 C₁₋₂-alkylamino,
 aminosulfonyl,
 C₃₋₆-cycloalkyl,
 30 cyano,
 C₁₋₂-hydroxyalkyl,
 nitro,
 C₂₋₃-alkenyl,

20046564-0100

C₂₋₃-alkynyl,
 C₁₋₆-haloalkoxy,
 C₁₋₆-carboxyalkyl,
 5-6-membered heterocyclyl-C₁₋₆-alkylamino,
 5 unsubstituted or substituted phenyl and
 unsubstituted or substituted 5-6 membered
 heterocyclyl;

wherein R⁴ is selected from a direct bond, C₁₋₄-alkyl, and



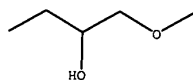
- 10 wherein R² is selected from C₁₋₂-alkyl, C₂₋₆-branched alkyl,
 C₂₋₄-branched haloalkyl, amino-C₁₋₄-alkyl and C₁₋₂-
 alkylamino-C₁₋₂-alkyl;
 wherein R^e and R^f are independently selected from H and C₁₋₂-
 haloalkyl; and
- 15 wherein R⁷ is selected from H, C₁₋₃-alkyl, optionally
 substituted phenyl, optionally substituted phenyl-C₁₋₃-
 alkyl, optionally substituted 4-6 membered
 heterocyclyl, optionally substituted 4-6 membered
 heterocyclyl-C₁₋₃-alkyl, C₁₋₃-alkoxy-C₁₋₂-alkyl and C₁₋₃-
 20 alkoxy-C₁₋₃-alkoxy-C₁₋₃-alkyl;
 and pharmaceutically acceptable isomers and derivatives
 thereof.

46. A compound of Claim 45 wherein R is selected from
- 25 4-pyridyl, 3-pyridyl, 2-pyridyl, pyrimidinyl, triazolyl,
 pyridazinyl, indolyl, isoindolyl, indazolyl, quinolyl,
 isoquinolyl, benzotriazolyl, naphthyridinyl and
 quinoxalinyl, where R is unsubstituted or substituted with
 one or more substituents selected from chloro, fluoro,
 30 amino, hydroxy, methyl, ethyl, propyl, trifluoromethyl,
 dimethylaminopropynyl, 1-methylpiperidinylmethoxy,
 dimethylaminoethoxyethoxy, methoxy and ethoxy; wherein R¹ is
 selected from 1,2-dihydroquinolyl, 1,2,3,4-tetrahydro-

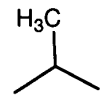
- isoquinolyl, 2,3-dihydro-1H-indolyl, dihydro-benzimidazolyl, benzo[d]isothiazolyl, 2,3,4,4a,9,9a-hexahydro-1H-3-aza-fluorenyl, 5,6,7-trihydro-1,2,4-triazolo[3,4-a]isoquinolyl, and tetrahydroquinolinyl, where R¹ is unsubstituted or
- 5 substituted with one or more substituents selected from bromo, chloro, fluoro, iodo, nitro, amino, cyano, aminoethyl, Boc-aminoethyl, hydroxy, oxo, aminosulfonyl, 4-methylpiperazinylsulfonyl, cyclohexyl, phenyl, phenylmethyl, morpholinylmethyl, 1-methylpiperazin-4-ylmethyl, 1-
- 10 methylpiperazin-4-ylpropyl, morpholinylpropyl, piperidin-1-ylmethyl, 1-methylpiperidin-4-ylmethyl, 2-methyl-2-(1-methylpiperidin-4-yl)ethyl, morpholinylethyl, 1-(4-morpholinyl)-2,2-dimethylpropyl, piperidin-4-ylethyl, 1-Boc-piperidin-4-ylethyl, piperidin-1-ylethyl, 1-Boc-piperidin-4-
- 15 ylethyl, piperidin-4-ylmethyl, 1-Boc-piperidin-4-ylmethyl, piperidin-4-ylpropyl, 1-Boc-piperidin-4-ylpropyl, piperidin-1-ylpropyl, pyrrolidin-1-ylpropyl, pyrrolidin-2-ylpropyl, 1-Boc-pyrrolidin-2-ylpropyl, pyrrolidin-1-ylmethyl, pyrrolidin-2-ylmethyl, 1-Boc-pyrrolidin-2-ylmethyl,
- 20 pyrrolidinylpropenyl, pyrrolidinylbutenyl, fluorosulfonyl, methylsulfonyl, methylcarbonyl, Boc, piperidin-1-ylmethylcarbonyl, 4-methylpiperazin-1-ylcarbonylethyl, methoxycarbonyl, aminomethylcarbonyl, dimethylaminomethylcarbonyl, 3-ethoxycarbonyl-2-methyl-fur-
- 25 5-yl, 4-methylpiperazin-1-yl, 4-methyl-1-piperidyl, 1-Boc-4-piperidyl, piperidin-4-yl, 1-methylpiperidin-4-yl, 1-methyl-(1,2,3,6-tetrahydropyridyl), imidazolyl, morpholinyl, 4-trifluoromethyl-1-piperidinyl, hydroxybutyl, methyl, ethyl, propyl, isopropyl, butyl, tert-butyl, sec-butyl,
- 30 trifluoromethyl, pentafluoroethyl, nonafluorobutyl, dimethylaminopropyl, 1,1-di(trifluoromethyl)-1-hydroxymethyl, 1,1-di(trifluoromethyl)-1-(piperidinylethoxy)methyl, 1,1-di(trifluoromethyl)-1-(methoxyethoxyethoxy)methyl, 1-hydroxyethyl, 2-hydroxyethyl,

"TOP SECRET" FOOTNOTES

- trifluoromethoxy, 1-aminoethyl, 2-aminoethyl, 1-(N-isopropylamino)ethyl, 2-(N-isopropylamino)ethyl, dimethylaminoethoxy, 4-chlorophenoxy, phenyloxy, azetidin-3-ylmethoxy, 1-Boc-azetidin-3-ylmethoxy, pyrrol-2-ylmethoxy, 1-Boc-pyrrol-2-ylmethoxy, pyrrol-1-ylmethoxy, 1-methyl-pyrrol-2-ylmethoxy, 1-isopropyl-pyrrol-2-ylmethoxy, 1-Boc-piperdin-4-ylmethoxy, piperdin-4-ylmethoxy, 1-methylpiperdin-4-yloxy, isopropoxy, methoxy and ethoxy; wherein R² is selected from H, chloro, fluoro, bromo, amino, hydroxy, methyl, ethyl, propyl, oxo, dimethylamino, aminosulfonyl, cyclopropyl, cyano, hydroxymethyl, nitro, propenyl, trifluoromethyl, methoxy, ethoxy, trifluoromethoxy, carboxymethyl, morpholinylethylamino, propynyl, unsubstituted or substituted phenyl and unsubstituted or substituted heteroaryl selected from thienyl, furanyl, pyridyl, imidazolyl, and pyrazolyl; wherein R⁴ is selected from a direct bond, ethyl, butyl, and

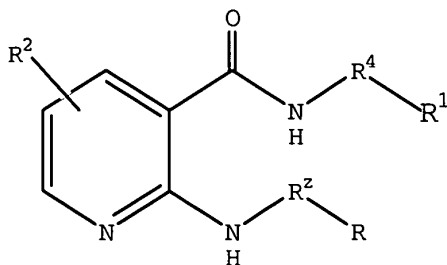


; and



- wherein R² is selected from methylenyl, ethylenyl, and aminoethylenyl; and pharmaceutically acceptable derivatives thereof.

47. A compound of Claim 1 having Formula XI

**XI**

wherein R is selected from

- a) unsubstituted or substituted 5- or 6-membered nitrogen-containing heteroaryl, and
- b) unsubstituted or substituted 9- or 10-membered fused heteroaryl,

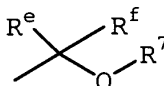
where substituted R is substituted with one or more substituents selected from halo, amino, hydroxy, C₁₋₆-alkyl, C₁₋₆-haloalkyl, C₁₋₆-alkoxy, optionally substituted heterocyclyl-C₁₋₆-alkoxy, optionally substituted heterocyclyl-C₁₋₆-alkylamino, optionally substituted heterocyclyl-C₁₋₆-alkyl, C₁₋₆-alkylamino-C₂₋₄-alkynyl, C₁₋₆-alkylamino-C₁₋₆-alkoxy, C₁₋₆-alkylamino-C₁₋₆-alkoxy-C₁₋₆-alkoxy, and optionally substituted heterocyclyl-C₂₋₄-alkynyl;

- 15 wherein R¹ is selected from unsubstituted or substituted aryl, cycloalkyl, 5-6 membered heteroaryl and 9-10 membered bicyclic and 13-14 membered tricyclic heterocyclyl,
- 20

wherein substituted R¹ is substituted with one or more substituents selected from halo, C₁₋₆-alkyl, optionally substituted C₃₋₆-cycloalkyl, optionally substituted phenyl, optionally substituted phenyl-C₁-C₄-alkylenyl, C₁₋₂-haloalkoxy, optionally substituted 4-6 membered heterocyclyl-C₁-C₄-alkyl, optionally substituted 4-6 membered heterocyclyl-C₂-C₄-alkenyl, optionally substituted 4-6 membered heterocyclyl, optionally substituted phenyloxy, optionally substituted 4-6 membered heterocyclyloxy, optionally substituted 4-6 membered heterocyclyl-C₁-C₄-alkoxy, optionally substituted 4-6 membered heterocyclylsulfonyl, optionally substituted 4-6 membered heterocyclylamino, optionally substituted 4-6 membered

Downloaded from ascel.org

heterocyclylcarbonyl, optionally substituted 5-6
 membered heterocyclyl-C₁₋₄-alkylcarbonyl, C₁₋₂-
 haloalkyl, C₁₋₄-aminoalkyl, nitro, amino, hydroxy,
 cyano, aminosulfonyl, C₁₋₂-alkylsulfonyl, halosulfonyl,
 5 C₁₋₄-alkylcarbonyl, C₁₋₃-alkylamino-C₁₋₃-alkyl, C₁₋₃-
 alkylamino-C₁₋₃-alkoxy, C₁₋₃-alkylamino-C₁₋₃-alkoxy-C₁₋₃-
 alkoxy, C₁₋₄-alkoxycarbonyl, C₁₋₄-alkoxycarbonylamino-C₁₋

4-alkyl, C₁₋₄-hydroxyalkyl,  and C₁₋₄-alkoxy;

wherein R² is one or more substituents independently

10 selected from

halo,

hydroxy,

amino,

C₁₋₆-alkyl,

15 C₁₋₆-haloalkyl,

C₁₋₆-alkoxy,

C₁₋₂-alkylamino,

aminosulfonyl,

C₃₋₆-cycloalkyl,

20 cyano,

C₁₋₂-hydroxyalkyl,

nitro,

C₂₋₃-alkenyl,

C₂₋₃-alkynyl,

25 C₁₋₆-haloalkoxy,

C₁₋₆-carboxyalkyl,

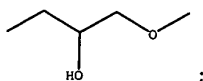
5-6-membered heterocyclyl-C₁₋₆-alkylamino,

unsubstituted or substituted phenyl and

unsubstituted or substituted 5-6 membered

30 heterocyclyl;

wherein R⁴ is selected from a direct bond, C₁₋₄-alkyl, and



wherein R^z is selected from C₁₋₂-alkyl, C₂₋₆-branched alkyl, C₂₋₄-branched haloalkyl, amino-C₁₋₄-alkyl and C₁₋₂-alkylamino-C₁₋₂-alkyl;

wherein R^e and R^f are independently selected from H and C₁₋₂-haloalkyl; and

wherein R⁷ is selected from H, C₁₋₃-alkyl, optionally substituted phenyl, optionally substituted phenyl-C₁₋₃-alkyl, optionally substituted 4-6 membered heterocyclyl, optionally substituted 4-6 membered heterocyclyl-C₁₋₃-alkyl, C₁₋₃-alkoxy-C₁₋₂-alkyl and C₁₋₃-alkoxy-C₁₋₃-alkoxy-C₁₋₃-alkyl;

and pharmaceutically acceptable isomers and derivatives thereof.

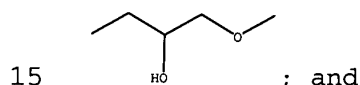
48. A compound of Claim 47 wherein R is selected from 4-pyridyl, 3-pyridyl, 2-pyridyl, pyrimidinyl, triazolyl, pyridazinyl, indolyl, isoindolyl, indazolyl, quinolyl, isoquinolyl, benzotriazolyl, naphthyridinyl and quinoxalinyl, where R is unsubstituted or substituted with one or more substituents selected from chloro, fluoro, amino, hydroxy, methyl, ethyl, propyl, trifluoromethyl, dimethylaminopropynyl, 1-methylpiperidinylmethoxy, dimethylaminoethoxyethoxy, methoxy and ethoxy; wherein R¹ is selected from phenyl, tetrahydronaphthyl, indanyl, indenyl, naphthyl, cyclohexyl, isoxazolyl, pyrazolyl, thiazolyl, thiadiazolyl, thienyl, pyridyl, pyrimidinyl, pyridazinyl, 1,2-dihydroquinolyl, 1,2,3,4-tetrahydro-isoquinolyl, isoquinolyl, quinolyl, indolyl, isoindolyl, 2,3-dihydro-1H-indolyl, naphthyridinyl, quinoxalinyl, benzo[d]isothiazolyl, 2,3,4,4a,9,9a-hexahydro-1H-3-aza-fluorenyl, 5,6,7-trihydro-1,2,4-triazolo[3,4-a]isoquinolyl, tetrahydroquinolinyl, indazolyl, 2,1,3-benzothiadiazolyl, benzodioxanyl, benzothienyl, benzofuryl, dihydro-benzimidazolyl, benzimidazolyl, benzoxazolyl and benzthiazolyl, where R¹ is

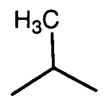
- unsubstituted or substituted with one or more substituents selected from bromo, chloro, fluoro, iodo, nitro, amino, cyano, aminoethyl, Boc-aminoethyl, hydroxy, oxo, aminosulfonyl, 4-methylpiperazinylsulfonyl, cyclohexyl,
- 5 phenyl, phenylmethyl, morpholinylmethyl, 1-methylpiperazin-4-ylmethyl, 1-methylpiperazin-4-ylpropyl, morpholinylpropyl, piperidin-1-ylmethyl, 1-methylpiperidin-4-ylmethyl, 2-methyl-2-(1-methylpiperidin-4-yl)ethyl, morpholinylethyl, 1-(4-morpholinyl)-2,2-dimethylpropyl, piperidin-4-ylethyl, 1-
- 10 Boc-piperidin-4-ylethyl, piperidin-1-ylethyl, 1-Boc-piperidin-4-ylethyl, piperidin-4-ylmethyl, 1-Boc-piperidin-4-ylmethyl, piperidin-4-ylpropyl, 1-Boc-piperidin-4-ylpropyl, piperidin-1-ylpropyl, pyrrolidin-1-ylpropyl, pyrrolidin-2-ylpropyl, 1-Boc-pyrrolidin-2-ylpropyl,
- 15 pyrrolidin-1-ylmethyl, pyrrolidin-2-ylmethyl, 1-Boc-pyrrolidin-2-ylmethyl, pyrrolidinylpropenyl, pyrrolidinylbutenyl, fluorosulfonyl, methylsulfonyl, methylcarbonyl, Boc, piperidin-1-ylmethylcarbonyl, 4-methylpiperazin-1-ylcarbonylethyl, methoxycarbonyl,
- 20 aminomethylcarbonyl, dimethylaminomethylcarbonyl, 3-ethoxycarbonyl-2-methyl-fur-5-yl, 4-methylpiperazin-1-yl, 4-methyl-1-piperidyl, 1-Boc-4-piperidyl, piperidin-4-yl, 1-methylpiperidin-4-yl, 1-methyl-(1,2,3,6-tetrahydropyridyl), imidazolyl, morpholinyl, 4-trifluoromethyl-1-piperidinyl,
- 25 hydroxybutyl, methyl, ethyl, propyl, isopropyl, butyl, tert-butyl, sec-butyl, trifluoromethyl, pentafluoroethyl, nonafluorobutyl, dimethylaminopropyl, 1,1-di(trifluoromethyl)-1-hydroxymethyl, 1,1-di(trifluoromethyl)-1-(piperidinylethoxy)methyl, 1,1-
- 30 di(trifluoromethyl)-1-(methoxyethoxyethoxy)methyl, 1-hydroxyethyl, 2-hydroxyethyl, trifluoromethoxy, 1-aminoethyl, 2-aminoethyl, 1-(N-isopropylamino)ethyl, 2-(N-isopropylamino)ethyl, dimethylaminoethoxy, 4-chlorophenoxy, phenyloxy, azetidin-3-ylmethoxy, 1-Boc-azetidin-3-ylmethoxy,

"EQUATE" TESTS

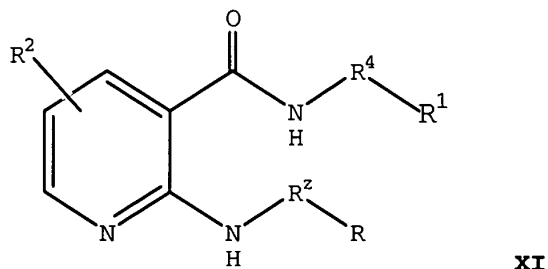
pyrrol-2-ylmethoxy, 1-Boc-pyrrol-2-ylmethoxy, pyrrol-1-ylmethoxy, 1-methyl-pyrrol-2-ylmethoxy, 1-isopropyl-pyrrol-2-ylmethoxy, 1-Boc-piperdin-4-ylmethoxy, piperdin-4-ylmethoxy, 1-methylpiperdin-4-yloxy, isopropoxy, methoxy and
 5 ethoxy; wherein R^2 is selected from chloro, fluoro, bromo, amino, hydroxy, methyl, ethyl, propyl, oxo, dimethylamino, aminosulfonyl, cyclopropyl, cyano, hydroxymethyl, nitro, propenyl, trifluoromethyl, methoxy, ethoxy, trifluoromethoxy, carboxymethyl, morpholinylethylamino,
 10 propynyl, unsubstituted or substituted phenyl and unsubstituted or substituted heteroaryl selected from thienyl,

furanyl, pyridyl, imidazolyl, and pyrazolyl;
 wherein R^4 is selected from a direct bond, ethyl, butyl, and



wherein R^z is selected from methylenyl, ethylenyl, ,
 and aminoethylenyl;
 and pharmaceutically acceptable derivatives thereof.

20 49. A compound of Claim 1 having Formula XI



wherein R is selected from

25 a) unsubstituted or substituted 5- or 6-membered nitrogen-containing heteroaryl, and

b) unsubstituted or substituted 9- or 10-membered fused heteroaryl,

where substituted R is substituted with one or more substituents selected from halo, amino, hydroxy, C₁₋₆-alkyl, C₁₋₆-haloalkyl, C₁₋₆-alkoxy, optionally substituted heterocyclyl-C₁₋₆-alkoxy, optionally substituted heterocyclyl-C₁₋₆-alkylamino, optionally substituted heterocyclyl-C₁₋₆-alkyl, C₁₋₆-alkylamino-C₂₋₄-alkynyl, C₁₋₆-alkylamino-C₁₋₆-alkoxy, C₁₋₆-alkylamino-C₁₋₆-alkoxy-C₁₋₆-alkoxy, and optionally substituted heterocyclyl-C₂₋₄-alkynyl;

wherein R¹ is selected from unsubstituted or substituted aryl, cycloalkyl, 5-6 membered heteroaryl and 9-10 membered bicyclic and 13-14 membered tricyclic heterocyclyl,

wherein substituted R¹ is substituted with one or more substituents selected from halo, C₁₋₆-alkyl, optionally substituted C₃₋₆-cycloalkyl, optionally substituted phenyl, optionally substituted phenyl-C₁.C₄-alkylenyl, C₁₋₂-haloalkoxy, optionally substituted 4-6 membered heterocyclyl-C₁.C₄-alkyl, optionally substituted 4-6 membered heterocyclyl-C₂.C₄-alkenyl, optionally substituted 4-6 membered heterocyclyl, optionally substituted phenyloxy, optionally substituted 4-6 membered heterocycliloxy, optionally substituted 4-6 membered heterocyclyl-C₁.C₄-alkoxy, optionally substituted 4-6 membered heterocyclylsulfonyl, optionally substituted 4-6 membered heterocyclylamino, optionally substituted 4-6 membered heterocyclylcarbonyl, optionally substituted 5-6 membered heterocyclyl-C₁₋₄-alkylcarbonyl, C₁₋₂-haloalkyl, C₁₋₄-aminoalkyl, nitro, amino, hydroxy,

2025 RELEASE UNDER E.O. 14176

wherein R^z is selected from C₁₋₂-alkyl, C₂₋₆-branched alkyl, C₂₋₄-branched haloalkyl, amino-C₁₋₄-alkyl and C₁₋₂-alkylamino-C₁₋₂-alkyl;

wherein R^e and R^f are independently selected from H and C₁₋₂-haloalkyl; and

wherein R⁷ is selected from H, C₁₋₃-alkyl, optionally substituted phenyl, optionally substituted phenyl-C₁₋₃-alkyl, optionally substituted 4-6 membered heterocyclyl, optionally substituted 4-6 membered heterocyclyl-C₁₋₃-alkyl, C₁₋₃-alkoxy-C₁₋₂-alkyl and C₁₋₃-alkoxy-C₁₋₃-alkoxy-C₁₋₃-alkyl;

provided R¹ is substituted with optionally substituted phenyloxy, optionally substituted 4-6 membered heterocyclyloxy, optionally substituted 4-6 membered heterocyclyl-C₁₋₄-alkoxy, optionally substituted 4-6 membered heterocyclylsulfonyl, optionally substituted 4-6 membered heterocyclylamino, optionally substituted 4-6 membered heterocyclylcarbonyl, optionally substituted 4-6 membered heterocyclyl-C₁₋₄-alkylcarbonyl, C₁₋₃-alkylamino-C₁₋₃-alkoxy, or C₁₋₃-alkylamino-C₁₋₃-alkoxy-C₁₋₃-alkoxy; further provided R is not 3-pyridyl when R⁵ is CH₂;

and pharmaceutically acceptable isomers and derivatives thereof.

50. A compound of Claim 49 wherein R is selected from 4-pyridyl, 3-pyridyl, 2-pyridyl, pyrimidinyl, triazolyl, pyridazinyl, indolyl, isoindolyl, indazolyl, quinolyl, isoquinolyl, benzotriazolyl, naphthyridinyl and quinoxalinyl, where R is unsubstituted or substituted with one or more substituents selected from chloro, fluoro, amino, hydroxy, methyl, ethyl, propyl, trifluoromethyl, dimethylaminopropynyl, 1-methylpiperidinylmethoxy, dimethylaminoethoxyethoxy, methoxy and ethoxy; wherein R¹ is

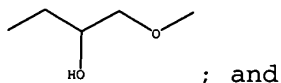
- selected from phenyl, tetrahydronaphthyl, indanyl, indenyl, naphthyl, cyclohexyl, isoxazolyl, pyrazolyl, thiazolyl, thiadiazolyl, thienyl, pyridyl, pyrimidinyl, pyridazinyl, 1,2-dihydroquinolyl, 1,2,3,4-tetrahydro-isoquinolyl, 5 isoquinolyl, quinolyl, indolyl, isoindolyl, 2,3-dihydro-1H-indolyl, naphthyridinyl, quinoxalinyl, benzo[d]isothiazolyl, 2,3,4,4a,9,9a-hexahydro-1H-3-aza-fluorenyl, 5,6,7-trihydro-1,2,4-triazolo[3,4-a]isoquinolyl, tetrahydroquinolinyl, indazolyl, 2,1,3-benzothiadiazolyl, benzodioxanyl, 10 benzothienyl, benzofuryl, benzimidazolyl, benzoxazolyl and benzthiazolyl, where R¹ is unsubstituted or substituted with one or more substituents selected from bromo, chloro, fluoro, iodo, nitro, amino, cyano, aminoethyl, Boc-aminoethyl, hydroxy, oxo, aminosulfonyl, 4- 15 methylpiperazinylsulfonyl, cyclohexyl, phenyl, phenylmethyl, morpholinylmethyl, 1-methylpiperazin-4-ylmethyl, 1-methylpiperazin-4-ylpropyl, morpholinylpropyl, piperidin-1-ylmethyl, 1-methylpiperidin-4-ylmethyl, 2-methyl-2-(1-methylpiperidin-4-yl)ethyl, morpholinylethyl, 1-(4- 20 morpholinyl)-2,2-dimethylpropyl, piperidin-4-ylethyl, 1-Boc-piperidin-4-ylethyl, piperidin-1-ylethyl, 1-Boc-piperidin-4-ylethyl, piperidin-4-ylmethyl, 1-Boc-piperidin-4-ylmethyl, piperidin-4-ylpropyl, 1-Boc-piperidin-4-ylpropyl, piperidin-1-ylpropyl, pyrrolidin-1-ylpropyl, pyrrolidin-2-ylpropyl, 1- 25 Boc-pyrrolidin-2-ylpropyl, pyrrolidin-1-ylmethyl, pyrrolidin-2-ylmethyl, 1-Boc-pyrrolidin-2-ylmethyl, pyrrolidinylpropenyl, pyrrolidinylbutenyl, fluorosulfonyl, methylsulfonyl, methylcarbonyl, Boc, piperidin-1-ylmethylcarbonyl, 4-methylpiperazin-1-ylcarbonylethyl, 30 methoxycarbonyl, aminomethylcarbonyl, dimethylaminomethylcarbonyl, 3-ethoxycarbonyl-2-methyl-fur-5-yl, 4-methylpiperazin-1-yl, 4-methyl-1-piperidyl, 1-Boc-4-piperidyl, piperidin-4-yl, 1-methylpiperidin-4-yl, 1-methyl-(1,2,3,6-tetrahydropyridyl), imidazolyl, morpholinyl, 4-

404554 0400
eoffo esof

- trifluoromethyl-1-piperidinyl, hydroxybutyl, methyl, ethyl, propyl, isopropyl, butyl, tert-butyl, sec-butyl, trifluoromethyl, pentafluoroethyl, nonafluorobutyl, dimethylaminopropyl, 1,1-di(trifluoromethyl)-1-
- 5 hydroxymethyl, 1,1-di(trifluoromethyl)-1-(piperidinylethoxy)methyl, 1,1-di(trifluoromethyl)-1-(methoxyethoxyethoxy)methyl, 1-hydroxyethyl, 2-hydroxyethyl, trifluoromethoxy, 1-aminoethyl, 2-aminoethyl, 1-(N-isopropylamino)ethyl, 2-(N-isopropylamino)ethyl,
- 10 dimethylaminoethoxy, 4-chlorophenoxy, phenyloxy, azetidin-3-ylmethoxy, 1-Boc-azetidin-3-ylmethoxy, pyrrol-2-ylmethoxy, 1-Boc-pyrrol-2-ylmethoxy, pyrrol-1-ylmethoxy, 1-methyl-pyrrol-2-ylmethoxy, 1-isopropyl-pyrrol-2-ylmethoxy, 1-Boc-piperdin-4-ylmethoxy, piperdin-4-ylmethoxy, 1-
- 15 methylpiperdin-4-yloxy, isopropoxy, methoxy and ethoxy; wherein R^2 is selected from H, chloro, fluoro, bromo, amino, hydroxy, methyl, ethyl, propyl, oxo, dimethylamino, aminosulfonyl, cyclopropyl, cyano, hydroxymethyl, nitro, propenyl, trifluoromethyl, methoxy, ethoxy,
- 20 trifluoromethoxy, carboxymethyl, morpholinylethylamino, propynyl, unsubstituted or substituted phenyl and unsubstituted or substituted heteroaryl selected from thienyl,

furanyl, pyridyl, imidazolyl, and pyrazolyl;

- 25 wherein R^4 is selected from a direct bond, ethyl, butyl, and

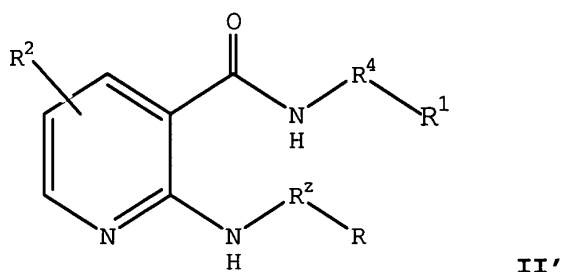


wherein R^2 is selected from methylenyl, ethylenyl, , and aminoethylenyl;

and pharmaceutically acceptable derivatives thereof.

30

51. A compound of Claim 1 having Formula II'



wherein R is selected from

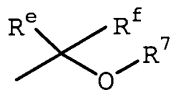
- 5 a) unsubstituted or substituted 5- or 6-membered non-nitrogen-containing heterocyclyl, and
 b) unsubstituted or substituted 9- or 10-membered fused partially unsaturated heterocyclyl,

10 where R is substituted with one or more substituents selected from halo, amino, hydroxy, C₁₋₆-alkyl, C₁₋₆-haloalkyl, C₁₋₆-alkoxy, optionally substituted heterocyclyl-C₁₋₆-alkoxy, optionally substituted heterocyclyl-C₁₋₆-alkylamino, optionally substituted heterocyclyl-C₁₋₆-alkyl, C₁₋₆-alkylamino-C₂₋₄-alkynyl, C₁₋₆-alkylamino-C₁₋₆-alkoxy, C₁₋₆-alkylamino-C₁₋₆-alkoxy-C₁₋₆-alkoxy, and optionally substituted heterocyclyl-C₂₋₄-alkynyl;

15 wherein R¹ is selected from unsubstituted or substituted aryl,
 20 cycloalkyl,
 5-6 membered heteroaryl and
 9-10 membered bicyclic and 13-14 membered tricyclic heterocyclyl,

 wherein substituted R¹ is substituted with one or more
 25 substituents selected from halo, C₁₋₆-alkyl, optionally substituted C₃₋₆-cycloalkyl, optionally substituted phenyl, optionally substituted phenyl-C_{1-C4}-alkylenyl, C₁₋₂-haloalkoxy, optionally substituted 4-6 membered heterocyclyl-C_{1-C4}-alkyl, optionally substituted 4-6

membered heterocyclyl-C₂-C₄-alkenyl, optionally
 substituted 4-6 membered heterocyclyl, optionally
 substituted phenyloxy, optionally substituted 4-6
 membered heterocyclxyloxy, optionally substituted 4-6
 5 membered heterocyclyl-C₁-C₄-alkoxy, optionally
 substituted 4-6 membered heterocyclylsulfonyl,
 optionally substituted 4-6 membered heterocyclylamino,
 optionally substituted 4-6 membered
 heterocyclylcarbonyl, optionally substituted 5-6
 10 membered heterocyclyl-C₁₋₄-alkylcarbonyl, C₁₋₂-
 haloalkyl, C₁₋₄-aminoalkyl, nitro, amino, hydroxy, oxo,
 -NHC(O)NH₂, alkylcarbonylamino, cyano, aminosulfonyl,
 C₁₋₂-alkylsulfonyl, halosulfonyl, C₁₋₄-alkylcarbonyl, C₁₋₃-
 alkylamino-C₁₋₃-alkyl, C₁₋₃-alkylamino-C₁₋₃-alkoxy, C₁₋₃-
 15 alkylamino-C₁₋₃-alkoxy-C₁₋₃-alkoxy, C₁₋₄-alkoxycarbonyl,
 C₁₋₄-alkoxycarbonylamino-C₁₋₄-alkyl, C₁₋₄-hydroxyalkyl,



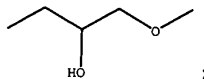
and C₁₋₄-alkoxy;

wherein R² is one or more substituents independently
 selected from

20 H,
 halo,
 hydroxy,
 amino,
 C₁₋₆-alkyl,
 25 C₁₋₆-haloalkyl,
 C₁₋₆-alkoxy,
 C₁₋₂-alkylamino,
 aminosulfonyl,
 C₃₋₆-cycloalkyl,
 30 cyano,
 C₁₋₂-hydroxyalkyl,
 nitro,
 C₂₋₃-alkenyl,

C₂₋₃-alkynyl,
 C₁₋₆-haloalkoxy,
 C₁₋₆-carboxyalkyl,
 5-6-membered heterocyclyl-C₁₋₆-alkylamino,
 5 unsubstituted or substituted phenyl and
 unsubstituted or substituted 5-6 membered
 heterocyclyl;

wherein R⁴ is selected from a direct bond, C₁₋₄-alkyl, and



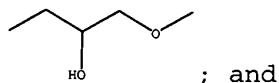
- 10 wherein R² is selected from C₁₋₂-alkyl, C₂₋₆-branched alkyl,
 C₂₋₄-branched haloalkyl, amino-C₁₋₄-alkyl and C₁₋₂-
 alkylamino-C₁₋₂-alkyl;
 wherein R^e and R^f are independently selected from H and C₁₋₂-
 haloalkyl; and
- 15 wherein R⁷ is selected from H, C₁₋₃-alkyl, optionally
 substituted phenyl-C₁₋₃-alkyl, optionally substituted
 4-6 membered heterocyclyl, optionally substituted 4-6
 membered heterocyclyl-C₁₋₃-alkyl, C₁₋₃-alkylamino-C₁₋₃-
 alkyl, C₁₋₃-alkoxy-C₁₋₂-alkyl and C₁₋₃-alkoxy-C₁₋₃-alkoxy-
 20 C₁₋₃-alkyl;
 and pharmaceutically acceptable isomers and derivatives
 thereof.

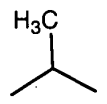
52. A compound of Claim 50 wherein R is selected from
- 25 2,3-dihydrobenzofuryl, and tetrahydropyran, where R is
 unsubstituted or substituted with one or more substituents
 selected from chloro, fluoro, amino, hydroxy, methyl, ethyl,
 propyl, trifluoromethyl, dimethylaminopropynyl, 1-
 methylpiperdinylmethoxy, dimethylaminoethoxyethoxy, methoxy
 30 and ethoxy; wherein R¹ is selected from phenyl,
 tetrahydronaphthyl, indanyl, indenyl, naphthyl, cyclohexyl,
 isoxazolyl, pyrazolyl, thiazolyl, thiadiazolyl, thienyl,
 pyridyl, pyrimidinyl, pyridazinyl, 1,2-dihydroquinolyl,

- 1,2,3,4-tetrahydro-isoquinolyl, isoquinolyl, quinolyl, indolyl, isoindolyl, 2,3-dihydro-1H-indolyl, naphthyridinyl, quinoxalinyl, benzo[d]isothiazolyl, 2,3,4,4a,9,9a-hexahydro-1H-3-aza-fluorenyl, 5,6,7-trihydro-1,2,4-triazolo[3,4-a]isoquinolyl, tetrahydroquinoliny, indazolyl, 2,1,3-benzothiadiazolyl, benzodioxanyl, benzothienyl, benzofuryl, benzimidazolyl, dihydro-benzimidazolyl, benzoxazolyl and benzthiazolyl, where R¹ is unsubstituted or substituted with one or more substituents selected from bromo, chloro, fluoro, iodo, nitro, amino, cyano, aminoethyl, Boc-aminoethyl, hydroxy, oxo, aminosulfonyl, 4-methylpiperazinylsulfonyl, cyclohexyl, phenyl, phenylmethyl, morpholinylmethyl, 1-methylpiperazin-4-ylmethyl, 1-methylpiperazin-4-ylpropyl, morpholinylpropyl, piperidin-1-ylmethyl, 1-methylpiperidin-4-ylmethyl, 2-methyl-2-(1-methylpiperidin-4-yl)ethyl, morpholinylethyl, 1-(4-morpholinyl)-2,2-dimethylpropyl, piperidin-4-ylethyl, 1-Boc-piperidin-4-ylethyl, piperidin-1-ylethyl, 1-Boc-piperidin-4-ylethyl, piperidin-4-ylmethyl, 1-Boc-piperidin-4-ylmethyl, piperidin-4-ylpropyl, 1-Boc-piperidin-4-ylpropyl, piperidin-1-ylpropyl, pyrrolidin-1-ylpropyl, pyrrolidin-2-ylpropyl, 1-Boc-pyrrolidin-2-ylpropyl, pyrrolidin-1-ylmethyl, pyrrolidin-2-ylmethyl, 1-Boc-pyrrolidin-2-ylmethyl, pyrrolidinylpropenyl, pyrrolidinylbutenyl, fluorosulfonyl, methylsulfonyl, methylcarbonyl, Boc, piperidin-1-ylmethylcarbonyl, 4-methylpiperazin-1-ylcarbonylethyl, methoxycarbonyl, aminomethylcarbonyl, dimethylaminomethylcarbonyl, 3-ethoxycarbonyl-2-methyl-fur-5-yl, 4-methylpiperazin-1-yl, 4-methyl-1-piperidyl, 1-Boc-4-piperidyl, piperidin-4-yl, 1-methylpiperidin-4-yl, 1-methyl-(1,2,3,6-tetrahydropyridyl), imidazolyl, morpholinyl, 4-trifluoromethyl-1-piperidinyl, hydroxybutyl, methyl, ethyl, propyl, isopropyl, butyl, tert-butyl, sec-butyl, trifluoromethyl, pentafluoroethyl, nonafluorobutyl,

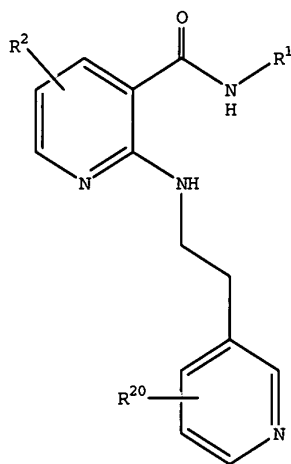
dimethylaminopropyl, 1,1-di(trifluoromethyl)-1-hydroxymethyl, 1,1-di(trifluoromethyl)-1-(piperidinylethoxy)methyl, 1,1-di(trifluoromethyl)-1-(methoxyethoxyethoxy)methyl, 1-hydroxyethyl, 2-hydroxyethyl, 5 trifluoromethoxy, 1-aminoethyl, 2-aminoethyl, 1-(N-isopropylamino)ethyl, 2-(N-isopropylamino)ethyl, dimethylaminoethoxy, 4-chlorophenoxy, phenyloxy, azetidin-3-ylmethoxy, 1-Boc-azetidin-3-ylmethoxy, pyrrol-2-ylmethoxy, 1-Boc-pyrrol-2-ylmethoxy, pyrrol-1-ylmethoxy, 1-methyl-10 pyrrol-2-ylmethoxy, 1-isopropyl-pyrrol-2-ylmethoxy, 1-Boc-piperdin-4-ylmethoxy, piperdin-4-ylmethoxy, 1-methylpiperdin-4-yloxy, isopropoxy, methoxy and ethoxy; wherein R² is selected from H, chloro, fluoro, bromo, amino, hydroxy, methyl, ethyl, propyl, oxo, dimethylamino, 15 aminosulfonyl, cyclopropyl, cyano, hydroxymethyl, nitro, propenyl, trifluoromethyl, methoxy, ethoxy, trifluoromethoxy, carboxymethyl, morpholinylethylamino, propynyl, unsubstituted or substituted phenyl and unsubstituted or substituted heteroaryl selected from 20 thienyl,

furanyl, pyridyl, imidazolyl, and pyrazolyl; wherein R⁴ is selected from a direct bond, ethyl, butyl, and



wherein R^z is selected from methylenyl, ethylenyl, , 25 and aminoethylenyl; and pharmaceutically acceptable derivatives thereof.

53. A compound of Claim 1 having Formula XII



XII

wherein R¹ is selected from unsubstituted or substituted
aryl,
5 cycloalkyl,
5-6 membered heteroaryl and
9-10 membered bicyclic and 13-14 membered tricyclic
heterocyclyl,

wherein substituted R¹ is substituted with one or more
10 substituents selected from halo, C₁-₆-alkyl, optionally
substituted C₃-₆-cycloalkyl, optionally substituted
phenyl, optionally substituted phenyl-C₁-C₄-alkylenyl,
C₁-₂-haloalkoxy, optionally substituted 4-6 membered
heterocyclyl-C₁-C₄-alkyl, optionally substituted 4-6
15 membered heterocyclyl-C₂-C₄-alkenyl, optionally
substituted 4-6 membered heterocyclyl, optionally
substituted phenyloxy, optionally substituted 4-6
membered heterocycliloxy, optionally substituted 4-6
membered heterocyclyl-C₁-C₄-alkoxy, optionally
20 substituted 4-6 membered heterocyclylsulfonyl,
optionally substituted 4-6 membered heterocyclylamino,
optionally substituted 4-6 membered
heterocyclylcarbonyl, optionally substituted 5-6
membered heterocyclyl-C₁-₄-alkylcarbonyl, C₁-₂-
25 haloalkyl, C₁-₄-aminoalkyl, nitro, amino, hydroxy,

optionally substituted 4-6 membered heterocyclyl-C₁-C₃-alkyl, C₁₋₃-alkoxy-C₁₋₂-alkyl and C₁₋₃-alkoxy-C₁₋₃-alkoxy-C₁₋₃-alkyl; and

wherein R²⁰ is one or more substituents selected from halo,

- 5 amino, hydroxy, C₁₋₆-alkyl, C₁₋₆-haloalkyl, C₁₋₆-alkoxy, optionally substituted heterocyclyl-C₁₋₆-alkoxy, optionally substituted heterocyclyl-C₁₋₆-alkylamino, optionally substituted heterocyclyl-C₁₋₆-alkyl, C₁₋₆-alkylamino-C₂₋₄-alkynyl, C₁₋₆-alkylamino-C₁₋₆-alkoxy, C₁₋₆-alkylamino-C₁₋₆-alkoxy-C₁₋₆-alkoxy, and optionally substituted heterocyclyl-C₂₋₄-alkynyl;
- 10

and pharmaceutically acceptable isomers and derivatives thereof.

- 15 54. Compound of Claim 53 wherein R¹ is selected from phenyl, tetrahydronaphthyl, indanyl, indenyl, naphthyl, cyclohexyl, isoxazolyl, pyrazolyl, thiazolyl, thiadiazolyl, thienyl, pyridyl, pyrimidinyl, pyridazinyl, 1,2-dihydroquinolyl, 1,2,3,4-tetrahydro-isoquinolyl, isoquinolyl, quinolyl, indolyl, isoindolyl, 2,3-dihydro-1H-indolyl, naphthyridinyl, quinoxalinyl, benzo[d]isothiazolyl, 2,3,4,4a,9,9a-hexahydro-1H-3-aza-fluorenyl, 5,6,7-trihydro-1,2,4-triazolo[3,4-a]isoquinolyl, tetrahydroquinolyl, indazolyl, 2,1,3-benzothiadiazolyl, benzodioxanyl, 20 benzothienyl, benzofuryl, dihydro-benzimidazolyl, benzimidazolyl, benzoxazolyl and benzthiazolyl, where R¹ is unsubstituted or substituted with one or more substituents selected from bromo, chloro, fluoro, iodo, nitro, amino, cyano, aminoethyl, Boc-aminoethyl, hydroxy, oxo, 25 aminosulfonyl, 4-methylpiperazinylsulfonyl, cyclohexyl, phenyl, phenylmethyl, morpholinylmethyl, 1-methylpiperazin-4-ylmethyl, 1-methylpiperazin-4-ylpropyl, morpholinylpropyl, piperidin-1-ylmethyl, 1-methylpiperidin-4-ylmethyl, 2-methyl-2-(1-methylpiperidin-4-yl)ethyl, morpholinylethyl, 1-
- 30

20040101 13:34:04

1. The first part of the report discusses the importance of maintaining accurate records of all transactions, including sales, purchases, and expenses. It emphasizes the need for a systematic approach to record-keeping, such as using a ledger or accounting software, to ensure that all data is captured and organized properly.

2. The second part of the report focuses on the importance of regular reconciliation. This involves comparing the company's internal records with external statements, such as bank statements or supplier invoices, to identify any discrepancies. Regular reconciliation helps to detect errors early and ensures that the company's financial records are accurate and up-to-date.

3. The third part of the report discusses the importance of maintaining proper documentation for all financial transactions. This includes keeping receipts, invoices, and other supporting documents for a sufficient period of time. Proper documentation is essential for auditing purposes and for ensuring the integrity of the company's financial records.

4. The fourth part of the report discusses the importance of maintaining accurate records of all assets and liabilities. This includes tracking the value of the company's property, equipment, and other assets, as well as its debts and obligations. Accurate records of assets and liabilities are essential for determining the company's net worth and for making informed financial decisions.

5. The fifth part of the report discusses the importance of maintaining accurate records of all income and expenses. This includes tracking the company's revenue from sales, as well as its operating expenses, such as salaries, rent, and utilities. Accurate records of income and expenses are essential for calculating the company's profit and for determining its tax liability.

6. The sixth part of the report discusses the importance of maintaining accurate records of all cash flows. This includes tracking the company's cash inflows from sales and other sources, as well as its cash outflows for operating expenses and capital expenditures. Accurate records of cash flows are essential for determining the company's liquidity and for making informed financial decisions.

7. The seventh part of the report discusses the importance of maintaining accurate records of all financial ratios and metrics. This includes calculating and tracking key financial ratios, such as the current ratio, the debt-to-equity ratio, and the return on equity. Accurate records of financial ratios and metrics are essential for evaluating the company's financial performance and for making informed financial decisions.

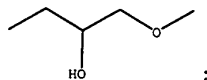
8. The eighth part of the report discusses the importance of maintaining accurate records of all financial statements. This includes preparing and maintaining the company's balance sheet, income statement, and cash flow statement. Accurate financial statements are essential for providing a clear and concise overview of the company's financial position and for making informed financial decisions.

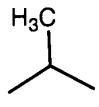
9. The ninth part of the report discusses the importance of maintaining accurate records of all financial transactions and statements for a sufficient period of time. This is typically determined by local laws and regulations, but it is generally recommended to keep records for at least seven years. Accurate records of financial transactions and statements are essential for auditing purposes and for ensuring the integrity of the company's financial records.

10. The tenth part of the report discusses the importance of maintaining accurate records of all financial transactions and statements for a sufficient period of time. This is typically determined by local laws and regulations, but it is generally recommended to keep records for at least seven years. Accurate records of financial transactions and statements are essential for auditing purposes and for ensuring the integrity of the company's financial records.

ethoxy, trifluoromethoxy, carboxymethyl, morpholinylethylamino, propynyl, unsubstituted or substituted phenyl and unsubstituted or substituted heteroaryl selected from thienyl,

- 5 furanyl, pyridyl, imidazolyl, and pyrazolyl; wherein R⁴ is selected from a direct bond, ethyl, butyl, and



wherein R² is selected from methylenyl, ethylenyl, , and aminoethylenyl; and

- 10 wherein R²⁰ is one or more substituents selected from chloro, fluoro, amino, hydroxy, methyl, ethyl, propyl, trifluoromethyl, dimethylaminopropynyl, 1-methylpiperidinylmethoxy, dimethylaminoethoxyethoxy, methoxy and ethoxy;
- 15 and pharmaceutically acceptable derivatives thereof.

55. Compound of Claim 1 and pharmaceutically acceptable derivatives thereof selected from

- 20 N-[3-(Isopropyl)phenyl]{2-[(4-pyridylmethyl)amino](3-pyridyl)}carboxamide;
- N-(3-Isoquinolyl){2-[(4-pyridylmethyl)amino](3-pyridyl)}carboxamide;
- 25 N-[4-Isopropylphenyl]{2-[(2-(3-pyridyl)ethyl)amino](3-pyridyl)}carboxamide;
- N-[4-(tert-Butyl)phenyl]{2-[(2-(3-pyridyl)ethyl)amino](3-pyridyl)}carboxamide;
- N-[4-(Methylpropyl)phenyl]{2-[(2-(3-pyridyl)ethyl)amino](3-pyridyl)}carboxamide;
- 30 {2-[(2-(3-Pyridyl)ethyl)amino](3-pyridyl)}-N-[3-(trifluoromethyl)phenyl]carboxamide;

THE

- N*-[2-(3-(Trifluoromethyl)phenyl)ethyl]-2-[(pyridin-4-ylmethyl)amino] (3-pyridyl)carboxamide;
- N*-[2-(3-Ethoxyphenyl)ethyl]-2-[(pyridin-4-ylmethyl)amino] (3-pyridyl)carboxamide;
- 5 *N*-[2-(3,4-Dimethylphenyl)ethyl]-2-[(pyridin-4-ylmethyl)amino] (3-pyridyl)carboxamide;
- N*-[2-(1,3-Benzodioxol-5-yl)ethyl]-2-[(pyridin-4-ylmethyl)amino] (3-pyridyl)carboxamide;
- N*-[2-(4-Methylphenyl)ethyl]-2-[(pyridin-4-ylmethyl)amino] (3-pyridyl)carboxamide;
- 10 *N*-[2-(4-Hydroxyphenyl)ethyl]-2-[(pyridin-4-ylmethyl)amino] (3-pyridyl)carboxamide;
- N*-[2-(3,4-Dimethoxyphenyl)ethyl]-2-[(pyridin-4-ylmethyl)amino] (3-pyridyl)carboxamide;
- 15 *N*-[2-(4-Bromophenyl)ethyl]-2-[(pyridin-4-ylmethyl)amino] (3-pyridyl)carboxamide;
- N*-[2-(3,4-Dichlorophenyl)ethyl]-2-[(pyridin-4-ylmethyl)amino] (3-pyridyl)carboxamide;
- N*-[2-(4-(Fluorosulfonyl)phenyl)ethyl]-2-[(pyridin-4-ylmethyl)amino] (3-pyridyl)carboxamide;
- 20 *N*-[2-(3,5-(Dimethoxy)phenyl)ethyl]-2-[(pyridin-4-ylmethyl)amino] (3-pyridyl)carboxamide;
- N*-[2-(2,4-Dichlorophenyl)ethyl]-2-[(pyridin-4-ylmethyl)amino] (3-pyridyl)carboxamide;
- 25 *N*-[2-(2-Fluorophenyl)ethyl]-2-[(pyridin-4-ylmethyl)amino] (3-pyridyl)carboxamide;
- N*-[2-(2-Chlorophenyl)ethyl]-2-[(pyridin-4-ylmethyl)amino] (3-pyridyl)carboxamide;
- N*-[2-(4-(Aminosulphonyl)phenyl)ethyl]-2-[(pyridin-4-ylmethyl)amino] (3-pyridyl)carboxamide;
- 30 *N*-[2-(2-Thienyl)ethyl]-2-[(pyridin-4-ylmethyl)amino] (3-pyridyl)carboxamide;
- N*-[2-(Pyridin-2-yl)ethyl]-2-[(pyridin-4-ylmethyl)amino] (3-pyridyl)carboxamide;

2004-10-13 13:54:04

- N-[2-(Pyridin-3-yl)ethyl]-2-[(pyridin-4-ylmethyl)amino] (3-pyridyl)carboxamide;
- N-[2-(Pyridin-4-yl)ethyl]-2-[(pyridin-4-ylmethyl)amino] (3-pyridyl)carboxamide;
- 5 N-(4-Phenylbutyl)-2-[(pyridin-4-ylmethyl)amino] (3-pyridyl)carboxamide;
- N-(2-Hydroxy-3-phenoxypropyl)-2-[(pyridin-4-ylmethyl)amino] (3-pyridyl)carboxamide;
- {6-Chloro-5-fluoro-2-[(4-pyridylmethyl)amino] (3-pyridyl)}-N-
- 10 [4-(isopropyl)phenyl]carboxamide;
- {5-Fluoro-2-[(4-pyridylmethyl)amino] (3-pyridyl)}-N-[4-(isopropyl)phenyl]carboxamide;
- 2-[(Pyridin-4-ylmethyl)amino]-N-[4-tert-butyl-3-(1,2,3,6-tetrahydropyridin-4-yl)phenyl] (3-pyridyl)carboxamide;
- 15 N-(3,4-Dichlorophenyl){6-[(2-morpholin-4-ylethyl)amino]-2-[(4-pyridylmethyl)amino] (3-pyridyl)}carboxamide;
- N-[4-(Morpholin-4-ylmethyl)phenyl]{2-[(4-pyridylmethyl)amino] (3-pyridyl)}carboxamide;
- N-(4-{2-[(tert-Butoxy)carbonylamino]ethyl}phenyl){2-[(4-pyridylmethyl)amino] (3-pyridyl)}carboxamide;
- 20 N-[4-(2-Aminoethyl)phenyl]{2-[(4-pyridylmethyl)amino] (3-pyridyl)}carboxamide;
- N-[4-(tert-Butyl)-3-nitrophenyl]{2-[(2-pyridylmethyl)amino] (3-pyridyl)}carboxamide;
- 25 N-[3-Amino-4-(tert-butyl)phenyl]{2-[(2-pyridylmethyl)amino] (3-pyridyl)}carboxamide;
- N-[4-(Isopropyl)phenyl]{2-[(2-pyridylmethyl)amino] (3-pyridyl)}carboxamide;
- N-(3-Aminosulfonyl-4-chlorophenyl){2-[(4-pyridylmethyl)amino] (3-pyridyl)}carboxamide;
- 30 N-{3-[(4-Methylpiperazinyl)sulfonyl]phenyl}{2-[(4-pyridylmethyl)amino] (3-pyridyl)}carboxamide;
- N-[4-(1,1,2,2,2-Pentafluoroethyl)phenyl]{2-[(4-pyridylmethyl)amino] (3-pyridyl)}carboxamide;

"TOP SECRET"

- N-[4-(1,1,2,2,3,3,4,4,4-Nonafluorobutyl)phenyl]{2-[(4-pyridylmethyl)amino](3-pyridyl)}carboxamide;
- N-[4-(Isopropyl)phenyl]{2-[(2-(1,2,4-triazolyl)ethyl)amino](3-pyridyl)}carboxamide;
- 5 (2-[(2-(2-Pyridylamino)ethyl)amino](3-pyridyl))-N-[3-(trifluoromethyl)phenyl]carboxamide;
- {2-[(1-(2-Pyridyl)pyrrolidin-3-yl)amino](3-pyridyl))-N-[3-(trifluoromethyl)phenyl]carboxamide;
- 2-[(Pyridin-4-ylmethyl)-amino]-N-(3-trifluoromethyl-phenyl)-
- 10 nicotinamide
- {2-[(4-Pyridylmethyl)amino](3-pyridyl))-N-(8-quinolyl)carboxamide hydrochloride;
- N-[4-(4-Chlorophenoxy)phenyl]{2-[(4-pyridylmethyl)amino](3-pyridyl)}carboxamide hydrochloride;
- 15 {2-[(4-Pyridylmethyl)amino](3-pyridyl))-N-(2,3,4-trifluorophenyl)carboxamide hydrochloride;
- N-(2-Naphthyl){2-[(4-pyridylmethyl)amino](3-pyridyl)}carboxamide hydrochloride;
- N-(2-Phenoxyphenyl){2-[(4-pyridylmethyl)amino](3-pyridyl)}carboxamide hydrochloride;
- 20 {2-[(4-Pyridylmethyl)amino](3-pyridyl))-N-(5,6,7,8-tetrahydronaphthyl)carboxamide hydrochloride;
- N-(2H-Benzo[3,4-d]1,3-dioxolen-5-yl){2-[(4-pyridylmethyl)amino](3-pyridyl)}carboxamide
- 25 hydrochloride;
- N-Naphthyl{2-[(4-pyridylmethyl)amino](3-pyridyl)}carboxamide hydrochloride;
- N-[3-Benzylphenyl]{2-[(4-pyridylmethyl)amino](3-pyridyl)}carboxamide hydrochloride;
- 30 N-(Cyclohexylethyl){2-[(4-pyridylmethyl)amino](3-pyridyl)}carboxamide hydrochloride;
- N-(Cyclohexylethyl){2-[(4-pyridylmethyl)amino](3-pyridyl)}carboxamide hydrochloride;

"SECRET"

- N-Indan-2-yl{2-[(4-pyridylmethyl)amino](3-pyridyl)}carboxamide hydrochloride;
- N-[4-(tert-Butyl)phenyl]{2-[(4-pyridylmethyl)amino](3-pyridyl)}carboxamide;
- 5 N-[4-(Methylpropyl)phenyl]{2-[(4-pyridylmethyl)amino](3-pyridyl)}carboxamide;
- Methylphenyl){2-[(4-pyridylmethyl)amino](3-pyridyl)}carboxamide;
- {2-[(4-Pyridylmethyl)amino](3-pyridyl)}-N-[4-trifluoromethoxy)phenyl]carboxamide;
- 10 N-(4-Ethylphenyl){2-[(4-pyridylmethyl)amino](3-pyridyl)}carboxamide;
- N-(4-Butylphenyl){2-[(4-pyridylmethyl)amino](3-pyridyl)}carboxamide;
- 15 N-(4-Iodophenyl){2-[(4-pyridylmethyl)amino](3-pyridyl)}carboxamide;
- N-[3-(Hydroxyethyl)phenyl]{2-[(4-pyridylmethyl)amino](3-pyridyl)}carboxamide;
- N-(3-Ethylphenyl){2-[(4-pyridylmethyl)amino](3-pyridyl)}carboxamide;
- 20 Ethyl 2-methyl-5-[3-({2-[(4-pyridylmethyl)amino](3-pyridyl)}carbonylamino)phenyl]furan-3-carboxylate;
- N-(3-Phenylphenyl){2-[(4-pyridylmethyl)amino](3-pyridyl)}carboxamide;
- 25 N-[4-Benzylphenyl]{2-[(4-pyridylmethyl)amino](3-pyridyl)}carboxamide;
- N-(6-Ethyl(2-pyridyl)){2-[(4-pyridylmethyl)amino](3-pyridyl)}carboxamide;
- N-(6-Propyl(2-pyridyl)){2-[(4-pyridylmethyl)amino](3-pyridyl)}carboxamide;
- 30 N-[4-(tert-Butyl)(2-pyridyl)]{2-[(4-pyridylmethyl)amino](3-pyridyl)}carboxamide;
- N-(3-Hydroxyphenyl){2-[(4-pyridylmethyl)amino](3-pyridyl)}carboxamide;

N-[3,5-bis(Trifluoromethyl)phenyl]{2-[(4-pyridylmethyl)amino](3-pyridyl)}carboxamide

N-[4-Chloro-3-(trifluoromethyl)phenyl]{2-[(4-pyridylmethyl)amino](3-pyridyl)}carboxamide hydrochloride;

N-(4-Phenoxyphenyl){2-[2-(2-pyridyl)ethyl]amino}(3-pyridyl)carboxamide;

15 N-(4-Phenoxyphenyl){2-[(2-(3-pyridyl)ethyl)amino](3-
pyridyl)}carboxamide;

N-(1-Acetylundolin-6-yl) (2-[(4-pyridylmethyl)amino] (3-
20 pyridyl)carboxamide;

N-Indol-6-yl(2-[(4-pyridylmethyl)amino](3-pyridyl))carboxamide;

N-Indol-7-yl{2-[(4-pyridylmethyl)amino](3-pyridyl)}carboxamide;

N-(3-Phenylpyrazol-5-yl){2-[(4-pyridylmethyl)amino](3-pyridyl)}carboxamide;

N-{2-[2-(dimethylamino)ethoxy]-5-(tert-butyl)phenyl}{2-[(4-pyridylmethyl)amino](3-pyridyl)}carboxamide;

- N-[4-(tert-Butyl)-3-(4-methylpiperazinyl)phenyl]{2-[(4-pyridylmethyl)amino](3-pyridyl)}carboxamide;
- N-[3-(4-Methylpiperazinyl)phenyl]{2-[(4-pyridylmethyl)amino](3-pyridyl)}carboxamide;
- 5 N-[4-(4-Methylpiperazinyl)phenyl]{2-[(4-pyridylmethyl)amino](3-pyridyl)}formamide;
- N-[1-(1-Methyl-(4-piperidyl))indolin-6-yl]{2-[(4-pyridylmethyl)amino](3-pyridyl)}carboxamide;
- N-[1-(1-Methyl-(4-piperidyl))indolin-6-yl]{2-[(2-(3-pyridyl)ethyl)amino](3-pyridyl)}carboxamide;
- 10 N-[1-(2-Piperidylethyl)indolin-6-yl]{2-[(4-pyridylmethyl)amino](3-pyridyl)}carboxamide;
- N-[1-(2-Piperidylacetyl)indolin-6-yl]{2-[(4-pyridylmethyl)amino](3-pyridyl)}carboxamide;
- 15 N-[3,3-Dimethyl-1-(1-methyl(4-piperidyl))indolin-6-yl]{2-[(4-pyridylmethyl)amino](3-pyridyl)}carboxamide;
- N-(3,3-Dimethylindolin-6-yl){2-[(4-pyridylmethyl)amino](3-pyridyl)}carboxamide;
- N-[3-(1-Methyl-(4-piperidyl))indol-5-yl]{2-[(4-pyridylmethyl)amino](3-pyridyl)}carboxamide;
- 20 N-[4-(1,1-Dimethyl-3-morpholin-4-ylpropyl)phenyl]{2-[(4-pyridylmethyl)amino](3-pyridyl)}carboxamide;
- N-[4-(tert-Butyl)phenyl]{2-[(2-[(1-methyl(4-piperidyl))-methoxy](4-pyridyl)methyl)amino](3-pyridyl)}carboxamide;
- 25 N-(4-Bromo-2-fluorophenyl){2-[(4-pyridylmethyl)amino](3-pyridyl)}carboxamide;
- N-[4-(tert-Butyl)phenyl]{2-[(2-chloro(4-pyridyl)methyl)amino](3-pyridyl)}carboxamide;
- {2-[(2-[3-(Dimethylamino)prop-1-ynyl](4-pyridyl)methyl)amino](3-pyridyl)}-N-[4-(tert-butyl)phenyl]carboxamide;
- 30 {2-[(2-Methoxy(4-pyridyl)methyl)amino](3-pyridyl)}-N-[4-(methylethyl)phenyl]carboxamide;

EUPH-10-1834001

- N-[3-[3-(Dimethylamino)propyl]-5-(trifluoromethyl)phenyl]-
{2-[(4-pyridylmethyl) amino] (3-pyridyl) }carboxamide;
N-[4-(tert-Butyl)-3-(3-piperidylpropyl)phenyl]{2-[(4-
pyridylmethyl) amino] (3-pyridyl) }carboxamide;
5 N-[4-(tert-Butyl)-3-(3-pyrrolidinylpropyl)phenyl]{2-[(4-
pyridylmethyl) amino] (3-pyridyl) }carboxamide;
N-[3-((1E)-4-Pyrrolidinylbut-1-enyl)-4-(tert-
butyl)phenyl]{2-[(4-pyridylmethyl) amino] (3-
pyridyl) }carboxamide;
10 N-[4-(tert-Butyl)-3-(3-morpholin-4-ylpropyl)phenyl]{2-[(4-
pyridylmethyl) amino] (3-pyridyl) }carboxamide;
N-[1-(2-Morpholin-4-ylethyl)indol-6-yl]{2-[(4-
pyridylmethyl) amino] (3-pyridyl) }carboxamide;
N-[4-(tert-Butyl)phenyl]{2-[(pyrimidin-4-ylmethyl) amino] (3-
15 pyridyl) }carboxamide;
N-(4-Chlorophenyl){2-[(pyrimidin-4-ylmethyl) amino] (3-
pyridyl) }carboxamide;
{2-[(Pyrimidin-4-ylmethyl) amino] (3-pyridyl) }-N-[3-
(trifluoromethyl)phenyl]carboxamide;
20 N-[4-(Isopropyl)phenyl]{4-[(4-pyridylmethyl) amino]pyrimidin-
5-yl}carboxamide;
(2-[[(2-[2-(Dimethylamino)ethoxy]ethoxy) (4-
pyridyl))methyl]amino) (3-pyridyl))-N-[4-(tert-
butyl)phenyl]carboxamide;
25 {2-[(4-Pyridylmethyl) amino] (3-pyridyl) }-N-[4-[2,2,2-
trifluoro-1-(2-piperidylethoxy)-1-
(trifluoromethyl)ethyl]phenyl]carboxamide;
(2-[[(2-[2-(Dimethylamino)ethoxy]ethoxy) (4-
pyridyl))methyl]amino)-6-fluoro(3-pyridyl))-N-[3-
30 (trifluoromethyl)phenyl]carboxamide;
N-[4-(tert-Butyl)phenyl]{6-fluoro-2-[(4-
pyridylmethyl) amino] (3-pyridyl) }carboxamide;
{6-Fluoro-2-[(4-pyridylmethyl) amino] (3-pyridyl) }-N-[4-
(isopropyl)phenyl]carboxamide;

"SECRET" 040994

- {6-Fluoro-2-[(4-pyridylmethyl)amino](3-pyridyl)}-N-[3-(trifluoromethyl)phenyl]carboxamide;
N-(1-Bromo(3-isoquinolyl)){6-fluoro-2-[(4-pyridylmethyl)amino](3-pyridyl)}-carboxamide;
5 N-(4-Phenoxyphenyl){2-[(4-pyridylmethyl)amino](3-pyridyl)}carboxamide hydrochloride;
N-(4-Phenylphenyl){2-[(4-pyridylmethyl)amino](3-pyridyl)}carboxamide hydrochloride;
N-(3-Phenoxyphenyl){2-[(4-pyridylmethyl)amino](3-pyridyl)}carboxamide hydrochloride;
10 N-(4-Cyclohexylphenyl){2-[(4-pyridylmethyl)amino](3-pyridyl)}carboxamide hydrochloride;
N-(4-Imidazol-1-ylphenyl){2-[(4-pyridylmethyl)amino](3-pyridyl)}carboxamide;
15 N-(4-Morpholin-4-ylphenyl){2-[(4-pyridylmethyl)amino](3-pyridyl)}carboxamide hydrochloride;
N-(4-Cyanonaphthyl){2-[(4-pyridylmethyl)amino](3-pyridyl)}carboxamide hydrochloride;
{2-[(4-Pyridylmethyl)amino](3-pyridyl)}-N-[4-(trifluoromethyl)phenyl]carboxamide hydrochloride;
20 Methyl-4-((2-[(4-pyridylmethyl)amino]-3-pyridyl)carbonylamino)benzoate hydrochloride;
N-[4-(Isopropyl)phenyl]{2-[(4-quinolylmethyl)amino](3-pyridyl)}carboxamide;
25 N-[4-(tert-Butyl)phenyl]{2-[(6-quinolylmethyl)amino](3-pyridyl)}carboxamide;
{2-[(6-quinolylmethyl)amino](3-pyridyl)}-N-[3-(trifluoromethyl)phenyl]carboxamide;
N-(4-chlorophenyl)-3-[(4-pyridinylmethylene)amino]-4-pyridinecarboxamide;
30 N-(4-chlorophenyl){3-[(4-pyridylmethyl)amino](2-thienyl)}carboxamide;
N-phenyl{3-[(4-pyridylmethyl)amino](2-thienyl)}carboxamide;

2025 RELEASE

- N-(4-chlorophenyl){2-[(4-pyridylmethyl)amino](3-pyridyl)}carboxamide;
- N-(3,4-dichlorophenyl){2-[(4-pyridylmethyl)amino](3-pyridyl)}-carboxamide;
- 5 N-(3-chlorophenyl){2-[(4-pyridylmethyl)amino](3-pyridyl)}carboxamide;
- N-(4-chlorophenyl){3-[(4-pyridylmethyl)amino](2-pyridyl)}carboxamide;
- N-(4-chlorophenyl){3-[(6-quinolylmethyl)amino](2-pyridyl)}carboxamide;
- 10 N-(3,4-dichlorophenyl){2-[(6-quinolylmethyl)amino](3-pyridyl)}-carboxamide;
- N-(4-chlorophenyl){6-methyl-2-[(4-pyridylmethyl)amino](3-pyridyl)}carboxamide;
- 15 N-(3,4-dichlorophenyl){6-methyl-2-[(4-pyridylmethyl)amino](3-pyridyl)}carboxamide;
- N-(3-fluoro-4-methylphenyl){6-methyl-2-[(4-pyridylmethyl)amino](3-pyridyl)}carboxamide;
- N-(3,4-dichlorophenyl){6-chloro-2-[(4-pyridylmethyl)amino](3-pyridyl)}carboxamide;
- 20 N-(4-chlorophenyl){6-chloro-2-[(4-pyridylmethyl)amino](3-pyridyl)}carboxamide;
- {6-chloro-2-[(4-pyridylmethyl)amino](3-pyridyl)}-N-(3-fluorophenyl)carboxamide;
- 25 N-(3-chlorophenyl){6-chloro-2-[(4-pyridylmethyl)amino](3-pyridyl)}carboxamide;
- N-(4-chlorophenyl){3-[(4-pyridylmethyl)amino](4-pyridyl)}carboxamide;
- N-(3-fluoro-4-methylphenyl){2-[(4-pyridylmethyl)amino](3-pyridyl)}carboxamide;
- 30 N-(4-chlorophenyl){2-[(4-quinolylmethyl)amino](3-pyridyl)}carboxamide;
- N-(4-chlorophenyl){2-[(5-quinolylmethyl)amino](3-pyridyl)}carboxamide;

- N-(4-chlorophenyl){2-[(4-pyridylethyl)amino]-5-(3-thienyl)-(3-pyridyl)}carboxamide;
- N-(4-chlorophenyl){5-(4-methoxyphenyl)-2-[(4-pyridylmethyl)amino]-(3-pyridyl)}carboxamide;
- 5 N-(4-chlorophenyl){5-bromo-2-[(4-pyridylmethyl)amino]-(3-pyridyl)}carboxamide;
- 2-[[2-(1-Isopropyl-azetidin-3-ylmethoxy)-pyridin-4-ylmethyl]-amino]-N-(4-trifluoromethyl-phenyl)-nicotinamide;
- 10 N-(4-tert-Butyl-phenyl)-2-[[2-(1-isopropyl-azetidin-3-ylmethoxy)-pyridin-4-ylmethyl]-amino]-nicotinamide;
- 2-[(2,3-Dihydro-benzofuran-5-ylmethyl)-amino]-N-{4-[1-methyl-1-(1-methyl-piperidin-4-yl)-ethyl]-phenyl}-nicotinamide;
- 15 N-(1-Acetyl-3,3-dimethyl-2,3-dihydro-1H-indol-6-yl)-2-[(2,3-dihydro-benzofuran-5-ylmethyl)-amino]-nicotinamide;
- 2-[(2,3-Dihydro-benzofuran-5-ylmethyl)-amino]-N-[3,3-dimethyl-1-(1-Boc-piperidin-4-ylmethyl)-2,3-dihydro-1H-indol-6-yl]-nicotinamide;
- 20 2-[(2,3-Dihydro-benzofuran-5-ylmethyl)-amino]-N-[3,3-dimethyl-1-(1-methylpiperidin-4-ylmethyl)-2,3-dihydro-1H-indol-6-yl]-nicotinamide;
- N-(1-Acetyl-3,3-dimethyl-2,3-dihydro-1H-indol-6-yl)-2-[(2-[2-(1-methyl-piperidin-4-yl)-ethoxy]-pyridin-4-ylmethyl)-amino]-nicotinamide;
- 25 2-[(2-[2-(1-Methyl-piperidin-4-yl)-ethoxy]-pyridin-4-ylmethyl)-amino]-N-(3-trifluoromethyl-phenyl)-nicotinamide;
- N-(4-tert-Butyl-phenyl)-2-[[2-ethylpyridin-4-ylmethyl]-amino]-nicotinamide;
- 30 N-(4-tert-Butyl-phenyl)-2-[(2-[2-(1-methyl-pyrrolidin-2-yl)-ethoxy]-pyridin-4-ylmethyl)-amino]-nicotinamide;

CONFIDENTIAL

- 2-({2-[2-(1-Methyl-pyrrolidin-2-yl)-ethoxy]-pyridin-4-ylmethyl}-amino)-N-(4-pentafluoroethyl-phenyl)-nicotinamide;
- 5 N-(4-Pentafluoroethyl-phenyl)-2-([2-(2-pyrrolidin-1-yl-ethoxy)-pyridin-4-ylmethyl]-amino)-nicotinamide;
- N-(4-tert-Butyl-phenyl)-2-([2-(2-pyrrolidin-1-yl-ethoxy)-pyridin-4-ylmethyl]-amino)-nicotinamide;
- N-[3-(4-Boc-piperazin-1-ylmethyl)-5-trifluoromethyl-phenyl]-2-[(pyridin-4-ylmethyl)-amino]-nicotinamide;
- 10 N-[3-(4-Boc-piperazine-1-carbonyl)-5-trifluoromethyl-phenyl]-2-[(pyridin-4-ylmethyl)-amino]-nicotinamide;
- N-[3-(4-Boc-piperazine-1-carbonyl)-5-trifluoromethyl-phenyl]-2-(2-pyridin-4-yl-ethylamino)-nicotinamide;
- N-[3-(4-Methyl-piperazin-1-ylmethyl)-4-pentafluoroethyl-phenyl]-2-[(pyridin-4-ylmethyl)-amino]-nicotinamide;
- 15 N-[3-(4-Boc-piperazin-1-ylmethyl)-4-pentafluoroethyl-phenyl]-2-[(pyridin-4-ylmethyl)-amino]-nicotinamide;
- 2-([2-(1-Methyl-piperidin-4-ylmethoxy)-pyridin-4-ylmethyl]-amino)-N-(4-trifluoromethyl-phenyl)-nicotinamide;
- 20 N-(4-tert-Butyl-phenyl)-2-([2-(1-methyl-piperidin-4-ylmethoxy)-pyridin-4-ylmethyl]-amino)-nicotinamide;
- 2-({2-[3-(1-Methyl-piperidin-4-yl)-propoxy]-pyridin-4-ylmethyl}-amino)-N-(4-pentafluoroethyl-phenyl)-nicotinamide;
- 25 N-(1-Acetyl-3,3-dimethyl-2,3-dihydro-1H-indol-6-yl)-2-[(2-methoxy-pyridin-4-ylmethyl)-amino]-nicotinamide;
- N-[3,3-Dimethyl-1-(1-methyl-piperidin-4-yl)-2,3-dihydro-1H-indol-6-yl]-2-[(2-methoxy-pyridin-4-ylmethyl)-amino]-nicotinamide;
- 30 N-(1-Boc-3,3-dimethyl-2,3-dihydro-1H-indol-6-yl)-2-[(2-methoxy-pyridin-4-ylmethyl)-amino]-nicotinamide;
- N-[3,3-Dimethyl-1-(1-Boc-piperidin-4-ylmethyl)-2,3-dihydro-1H-indol-6-yl]-2-[(2-methoxy-pyridin-4-ylmethyl)-amino]-nicotinamide;

"04100" 10045504

- N-[3,3-Dimethyl-1-(1-methyl-piperidin-4-yl)-2,3-dihydro-1H-indol-6-yl]-2-[(2-methoxy-pyridin-4-ylmethyl)-amino]-nicotinamide;
- 5 N-[1-(2-Dimethylamino-acetyl)-3,3-dimethyl-2,3-dihydro-1H-indol-6-yl]-2-[(2-methoxy-pyridin-4-ylmethyl)-amino]-nicotinamide;
- N-[1-(2-Dimethylamino-acetyl)-3,3-dimethyl-2,3-dihydro-1H-indol-6-yl]-2-[(pyridin-4-ylmethyl)-amino]-nicotinamide;
- 10 2-[(2-Methoxy-pyridin-4-ylmethyl)-amino]-N-[3-(1-Boc-piperidin-4-ylmethoxy)-5-trifluoromethyl-phenyl]-nicotinamide;
- N-[3,3-Dimethyl-1-(1-Boc-pyrrolidin-2-ylmethoxy)-2,3-dihydro-1H-indol-6-yl]-2-[(2-methoxy-pyridin-4-ylmethyl)-amino]-nicotinamide;
- 15 N-[3,3-Dimethyl-1-(2-Boc-amino-acetyl)-2,3-dihydro-1H-indol-6-yl]-2-[(2-methoxy-pyridin-4-ylmethyl)-amino]-nicotinamide;
- N-[3,3-Dimethyl-1-(2-Boc-amino-acetyl)-2,3-dihydro-1H-indol-6-yl]-2-[(pyridin-4-ylmethyl)-amino]-nicotinamide;
- 20 2-[(2-Methoxy-pyridin-4-ylmethyl)-amino]-N-[3-(1-methyl-pyrrolidin-2-ylmethoxy)-5-trifluoromethyl-phenyl]-nicotinamide;
- 2-[(2-Methoxy-pyridin-4-ylmethyl)-amino]-N-[3-(1-Boc-piperidin-4-ylmethyl)-5-trifluoromethyl-phenyl]-nicotinamide;
- 25 2-[(2-Methoxy-pyridin-4-ylmethyl)-amino]-N-[3-(4-Boc-piperazin-1-ylmethyl)-5-trifluoromethyl-phenyl]-nicotinamide;
- 30 2-{[2-(3-Morpholin-4-yl-propoxy)-pyridin-4-ylmethyl]-amino}-N-(4-pentafluoroethyl-phenyl)-nicotinamide;
- (S) 2-{[2-(1-Methyl-pyrrolidin-2-ylmethoxy)-pyridin-4-ylmethyl]-amino}-N-(4-pentafluoroethyl-phenyl)-nicotinamide;

2025 RELEASE UNDER E.O. 14176

- N-(3-tert-Butyl-isoxazol-5-yl)-2-{{2-(3-morpholin-4-yl-propoxy)-pyridin-4-ylmethyl}-amino}-nicotinamide;
N-(1-Acetyl-3,3-dimethyl-2,3-dihydro-1H-indol-6-yl)-2-{{2-(3-morpholin-4-yl-propylamino)-pyridin-4-ylmethyl}-amino}-nicotinamide;
5 N-(4-tert-Butyl-phenyl)-2-{{2-(3-morpholin-4-yl-propoxy)-pyridin-4-ylmethyl}-amino}-nicotinamide;
N-(4-tert-Butyl-phenyl)-2-{{2-(2-morpholin-4-yl-ethoxy)-pyridin-4-ylmethyl}-amino}-nicotinamide;
10 2-{{2-(2-Morpholin-4-yl-ethoxy)-pyridin-4-ylmethyl}-amino}-N-(4-trifluoromethyl-phenyl)-nicotinamide;
2-{{2-(2-Morpholin-4-yl-ethoxy)-pyridin-4-ylmethyl}-amino}-N-(3-trifluoromethyl-phenyl)-nicotinamide;
2-{{2-(2-Morpholin-4-yl-ethoxy)-pyridin-4-ylmethyl}-amino}-N-(4-pentafluoroethyl-phenyl)-nicotinamide;
15 N-(3-tert-Butyl-isoxazol-5-yl)-2-{{2-(2-morpholin-4-yl-ethoxy)-pyridin-4-ylmethyl}-amino}-nicotinamide;
N-(1-Acetyl-3,3-dimethyl-2,3-dihydro-1H-indol-6-yl)-2-{{2-(2-morpholin-4-yl-ethoxy)-pyridin-4-ylmethyl}-amino}-nicotinamide;
20 N-(1-Acetyl-3,3-dimethyl-2,3-dihydro-1H-indol-6-yl)-2-{{2-(1-methyl-piperidin-4-yloxy)-pyridin-4-ylmethyl}-amino}-nicotinamide;
2-{{2-(1-Methyl-piperidin-4-yloxy)-pyridin-4-ylmethyl}-amino}-N-(4-trifluoromethyl-phenyl)-nicotinamide;
25 2-{{2-(1-Methyl-piperidin-4-yloxy)-pyridin-4-ylmethyl}-amino}-N-(4-pentafluoroethyl-phenyl)-nicotinamide;
2-{{2-(1-Methyl-piperidin-4-yloxy)-pyridin-4-ylmethyl}-amino}-N-(4-tert-butyl-phenyl)-nicotinamide;
30 (R) N-(4-tert-Butyl-phenyl)-2-{{2-(1-methyl-pyrrolidin-2-ylmethoxy)-pyridin-4-ylmethyl}-amino}-nicotinamide;
(R) N-[3-(1-Boc-pyrrolidin-2-ylmethoxy)-5-trifluoromethyl-phenyl]-2-[(pyridin-4-ylmethyl)-amino]-nicotinamide;

"SECRET" 040604

- (R) N-[3-(1-Methyl-pyrrolidin-2-ylmethoxy)-5-trifluoromethyl-phenyl]-2-[(pyridin-4-ylmethyl)-amino]-nicotinamide;
- 5 N-[3-(1-Methyl-piperidin-4-yloxy)-5-trifluoromethyl-phenyl]-2-[(pyridin-4-ylmethyl)-amino]-nicotinamide;
- N-[3-(1-Methyl-piperidin-4-ylmethyl)-5-trifluoromethyl-phenyl]-2-[(pyridin-4-ylmethyl)-amino]-nicotinamide;
- 10 N-[3-tert-Butyl-4-(1-Boc-pyrrolidin-2-ylmethoxy)-phenyl]-2-[(pyridin-4-ylmethyl)-amino]-nicotinamide;
- N-(3,3-Dimethyl-2,3-dihydro-benzofuran-6-yl)-2-{{2-(1-methyl-piperidin-4-ylmethoxy)-pyridin-4-ylmethyl}-amino}-nicotinamide;
- 15 2-{{2-[3-(1-Methyl-piperidin-4-yl)-propoxy]-pyridin-4-ylmethyl}-amino)-N-(4-trifluoromethyl-phenyl)-nicotinamide;
- 2-{{2-[3-(1-Methyl-piperidin-4-yl)-propoxy]-pyridin-4-ylmethyl}-amino)-N-(3-trifluoromethyl-phenyl)-nicotinamide;
- 20 2-{{2-[3-(1-Methyl-piperidin-4-yl)-propoxy]-pyridin-4-ylmethyl}-amino)-N-(4-tert-butyl-phenyl)-nicotinamide;
- 2-{{2-[3-(1-Methyl-piperidin-4-yl)-propoxy]-pyridin-4-ylmethyl}-amino)-N-(3-tert-butyl-isoxazol-5-yl)-nicotinamide;
- 25 N-(3,3-Dimethyl-2,3-dihydro-1H-indol-6-yl)-2-{{2-[3-(1-methyl-piperidin-4-yl)-propoxy]-pyridin-4-ylmethyl}-amino}-nicotinamide;
- 2-[(Pyridin-4-ylmethyl)-amino]-N-(3,9,9-trimethyl-2,3,4,4a,9,9a-hexahydro-1H-3-aza-fluoren-6-yl)-nicotinamide;
- 30 N-[3,3-Dimethyl-1-(1-Boc-piperidin-4-ylmethyl)-2,3-dihydro-1H-indol-6-yl]-2-[(pyridin-4-ylmethyl)-amino]-nicotinamide;

"SECRET"

- N-[3,3-Dimethyl-1-(1-methyl-piperidin-4-ylmethyl)-2,3-dihydro-1H-indol-6-yl]-2-[(pyridin-4-ylmethyl)-amino]-nicotinamide;
- 2-[[2-(1-Methyl-piperidin-4-ylmethoxy)-pyridin-4-ylmethyl]-amino]-N-(4-pentafluoroethyl-phenyl)-nicotinamide;
- 5 N-(3-tert-Butyl-isoxazol-5-yl)-2-[[2-(1-methyl-piperidin-4-ylmethoxy)-pyridin-4-ylmethyl]-amino]-nicotinamide;
- N-(1-Acetyl-3,3-dimethyl-2,3-dihydro-1H-indol-6-yl)-2-[[2-(1-methyl-piperidin-4-ylmethoxy)-pyridin-4-ylmethyl]-amino]-nicotinamide;
- 10 N-(4-tert-Butyl-phenyl)-2-[[2-(3-morpholin-4-yl-propylamino)-pyrimidin-4-ylmethyl]-amino]-nicotinamide;
- 2-[[2-(3-Morpholin-4-yl-propylamino)-pyrimidin-4-ylmethyl]-amino]-N-(4-pentafluoroethyl-phenyl)-nicotinamide;
- 15 2-[[2-(3-Morpholin-4-yl-propylamino)-pyrimidin-4-ylmethyl]-amino]-N-(3-trifluoromethyl-phenyl)-nicotinamide;
- N-(4-tert-Butyl-phenyl)-2-([2-[2-(1-methyl-pyrrolidin-2-yl)-ethylamino]-pyrimidin-4-ylmethyl]-amino)-nicotinamide;
- 20 N-(1-Acetyl-3,3-dimethyl-2,3-dihydro-1H-indol-6-yl)-2-([2-[2-(1-methyl-pyrrolidin-2-yl)-ethylamino]-pyrimidin-4-ylmethyl]-amino)-nicotinamide;
- 2-[[2-(1-Methyl-piperidin-4-ylmethoxy)-pyridin-4-ylmethyl]-amino]-N-[3-(1-methyl-piperidin-4-yl)-5-trifluoromethyl-phenyl]-nicotinamide;
- 25 N-(3-tert-Butyl-isoxazol-5-yl)-2-[[2-(1-methyl-piperidin-4-ylmethoxy)-pyridin-4-ylmethyl]-amino]-nicotinamide;
- N-[3-(1-Boc-azetidin-3-ylmethoxy)-5-trifluoromethyl-phenyl]-2-[(pyridin-4-ylmethyl)-amino]-nicotinamide;
- 30 2-[(2-Methoxy-pyridin-4-ylmethyl)-amino]-N-[3-(1-Boc-azetidin-3-ylmethoxy)-5-trifluoromethyl-phenyl]-nicotinamide;
- 2-[(Pyridin-4-ylmethyl)-amino]-N-(2,2,4-trimethyl-3,4-dihydro-2H-benzo[1,4]oxazin-6-yl)-nicotinamide;

- N-(4-Acetyl-2,2-dimethyl-3,4-dihydro-2H-benzo[1,4]oxazin-6-yl)-2-[(pyridin-4-ylmethyl)-amino]-nicotinamide;
- N-(2,2-Dimethyl-3-oxo-3,4-dihydro-2H-benzo[1,4]oxazin-6-yl)-2-[(pyridin-4-ylmethyl)-amino]-nicotinamide;
- 5 2-[[2-(1-Benzhydryl-azetidin-3-yloxy)-pyridin-4-ylmethyl]-amino]-N-(4-tert-butyl-phenyl)-nicotinamide.
- N-(4,4-Dimethyl-1-oxo-1,2,3,4-tetrahydro-isoquinolin-7-yl)-2-[(pyridin-4-ylmethyl)-amino]-nicotinamide;
- N-(4-tert-Butyl-phenyl)-2-((2-[2-(1-methyl-piperidin-4-yl)-ethoxy]-pyridin-4-ylmethyl)-amino)-nicotinamide;
- 10 N-(3-tert-Butyl-isoxazol-5-yl)-2-((2-[2-(1-methyl-piperidin-4-yl)-ethoxy]-pyridin-4-ylmethyl)-amino)-nicotinamide;
- N-(3-trifluoromethylphenyl)-2-((2-[2-(1-methyl-piperidin-4-yl)-ethoxy]-pyridin-4-ylmethyl)-amino)-nicotinamide;
- 15 2-[(2,3-Dihydro-benzofuran-6-ylmethyl)-amino]-N-[3-(1-Boc-pyrrolidin-2-ylmethoxy)-4-pentafluoroethyl-phenyl]-nicotinamide;
- (R) N-[3-(2-Hydroxy-3-pyrrolidin-1-yl-propoxy)-4-pentafluoroethyl-phenyl]-2-[(pyridin-4-ylmethyl)-amino]-nicotinamide;
- 20 (S) N-[3-(2-Hydroxy-3-pyrrolidin-1-yl-propoxy)-4-pentafluoroethyl-phenyl]-2-[(pyridin-4-ylmethyl)-amino]-nicotinamide;
- N-[4-tert-Butyl-3-(1-methyl-piperidin-4-ylmethoxy)-phenyl]-2-[(pyridin-4-ylmethyl)-amino]-nicotinamide;
- 25 N-[3-(1-Methyl-piperidin-4-ylmethoxy)-4-pentafluoroethyl-phenyl]-2-[(pyridin-4-ylmethyl)-amino]-nicotinamide;
- N-[4-Pentafluoroethyl-3-(2-piperidin-1-yl-ethoxy)-phenyl]-2-[(pyridin-4-ylmethyl)-amino]-nicotinamide;
- 30 N-[4-Trifluoromethyl-3-(2-piperidin-1-yl-ethoxy)-phenyl]-2-[(pyridin-4-ylmethyl)-amino]-nicotinamide;
- (S) N-[3-(1-Boc-pyrrolidin-2-ylmethoxy)-4-pentafluoroethyl-phenyl]-2-[(pyridin-4-ylmethyl)-amino]-nicotinamide;

"SECRET" 000000

- (R) N-[3-(1-Boc-pyrrolidin-2-ylmethoxy)-4-trifluoromethyl-phenyl]-2-[(pyridin-4-ylmethyl)-amino]-nicotinamide;
- (R) N-[3-(1-Boc-pyrrolidin-2-ylmethoxy)-4-pentafluoroethyl-phenyl]-2-[(pyridin-4-ylmethyl)-amino]-nicotinamide;
- 5 N-(4-tert-Butyl-phenyl)-2-{{2-(1-methyl-piperidin-4-yloxy)-pyridin-4-ylmethyl}-amino}-nicotinamide; N-(3-Trifluoromethyl-phenyl)-2-{{2-(1-methyl-piperidin-4-yloxy)-pyridin-4-ylmethyl}-amino}-nicotinamide;
- 10 Cu) N-(3-tert-Butyl-isoxazol-5-yl)-2-{{2-(1-methyl-piperidin-4-yloxy)-pyridin-4-ylmethyl}-amino}-nicotinamide was prepared with pyridine and TEA at 90C.
- N-[3-(3-Piperidin-1-yl-propyl)-5-trifluoromethyl-phenyl]-2-[(pyridin-4-ylmethyl)-amino]-nicotinamide ;
- 15 N-[3-(3-Morpholin-4-yl-propyl)-5-trifluoromethyl-phenyl]-2-[(pyridin-4-ylmethyl)-amino]-nicotinamide;
- 2-[2-Methoxy-pyridin-4-ylmethyl)-amino]-N-[3-(1-Boc-piperidin-4-yloxy)-5-trifluoromethyl-phenyl]-nicotinamide;
- 20 N-{4-tert-Butyl-3-[2-(1-Boc-piperidin-4-yl)-ethyl]-phenyl}-2-[(pyridin-4-ylmethyl)-amino]-nicotinamide ;
- N-[4-tert-Butyl-3-(1-methyl-azetidin-3-ylmethoxy)-phenyl]-2-[(pyridin-4-ylmethyl)-amino]-nicotinamide;
- N-(3,3-Dimethyl-1,1-dioxo-2,3-dihydro-1H-1λ-
- 25 benzo[d]isothiazol-6-yl)-2-[(pyridin-4-ylmethyl)-amino]-nicotinamide;
- N-[1,1,4,4-Tetramethyl-1,2,3,4-tetrahydro-naphth-6-yl]-2-[(pyridin-4-ylmethyl)-amino]-nicotinamide;
- N-{4-[1-Methyl-1-(1-methyl-piperidin-4-yl)-ethyl]-phenyl}-2-
- 30 [(pyridin-4-ylmethyl)-amino]-nicotinamide;
- 2-[2-Methoxy-pyridin-4-ylmethyl)-amino]-N-{4-[1-methyl-1-(1-methyl-piperidin-4-yl)-ethyl]-phenyl}-nicotinamide;
- N-(3,3-Dimethyl-2,3-dihydro-benzofuran-6-yl)-2-[(pyridin-4-ylmethyl)-amino]-nicotinamide;

CONFIDENTIAL

SECRET

N-(3,3-dimethyl-2,3-dihydro-1H-indol-6-yl)-2-{[2-(2-morpholin-4-yl-propoxy)-pyridin-4-ylmethyl]-amino}-nicotinamide;

2-([2-(Azetidin-3-yloxy)-pyridin-4-ylmethyl]-amino)-N-(4-tert-butyl-phenyl)nicotinamide;

N-[3,3-Dimethyl-1,1-dioxo-2-(2-piperidin-1-yl-ethyl)-2,3-dihydro-1H-1λ'-benzo[d]isothiazol-6-yl]-2-[(pyridin-4-ylmethyl)-amino]-nicotinamide; and

N-[2-(2-Dimethylamino-ethyl)-3,3-dimethyl-1,1-dioxo-2,3-dihydro-1H-1λ'-benzo[d]isothiazol-6-yl]-2-[(pyridin-4-ylmethyl)-amino]-nicotinamide.

56. Compound of Claim 1 wherein ring A is selected from dihydropyran, dihydrothienyl, dihydrofuryl, oxo-dihydrofuryl, pyrrolinyl, dihydrothiazolyl, dihydro-oxazolyl, dihydro-isothiazolyl, dihydro-isoxazolyl, imidazolinyl, pyrazolinyl, triazinyl, thienyl, furanyl, pyrrolyl, thiazolyl, oxazolyl, imidazolyl, pyrazolyl, isoxazolyl, triazolyl and isothiazolyl.

57. Compound of Claim 1 wherein R is selected from substituted or unsubstituted, saturated or partially saturated 5-6 membered heterocycllyl, and substituted or unsubstituted saturated or partially saturated fused 9-, 10- or 11-membered heterocycllyl.

58. Compound of Claim 1 wherein R¹ is selected from

- a) substituted or unsubstituted saturated or partially saturated 5-6 membered heterocyclyl, and
- b) substituted or unsubstituted saturated or partially saturated 9-11 membered fused heterocyclyl.

59. Compound of Claim 58 wherein A is pyridyl.

60. Compound of Claim 1 wherein R¹ is selected from non-nitrogen-containing heteroaryl.

61. Compound of Claim 60 wherein R¹ is selected from pyranyl, furyl, thienyl, benzofuryl, and benzothienyl.

62. Compound of Claim 1 wherein R¹ is substituted with a substituent selected from -OR³, -SR³, -SO₂R³, -CONHR³, -COR³, -NHR³, -SO₂NHR³, -NHC(O)OR³, -NHC(O)R³ and optionally substituted 5-6 membered heterocyclyl-C₁-C₂-alkylenyl; and wherein R³ is selected from 5-6 membered heterocyclyl.